PHYSIOLOGICAL SCIENCES IN INDIA
Foundations and Frontiers

Edited by
K.N. SHARMA, FNA

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INDIAN NATIONAL SCIENCE ACADEMY
Bahadur Shah Zafar Marg, New Delhi 110 002

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Preface

The INSA National Committee on Physiology with the active help and participation of some eminent Indian scientists have attempted to bring out the present Status of Physiological Sciences in the country to particularly emphasize the current and emerging trends in thrust areas and in which Indian scientists have significantly contributed both at national and international level. While global perspectives are kept in mind, the highlights of the contributions made by different laboratories of India have been attempted to be put together and brought out in a cohesive manner. It is realised that the information gathered is not exhaustive and may not have covered certain important publications: this is entirely unintentional, and regretted for any such lapses. Also, there has been no exact cut-off date for coverage of the research work. Rather the genesis and development of the particular field of research in the country has been briefly touched upon, and dovetailed with the details of the work undertaken in recent years.

The contributors to the various Sections have readily responded to the request and are acknowledged leaders in the special areas of their work. Considerable liberty has been taken to add/delete/modify portions of the manuscripts to bring about uniformity in the write-ups; and of necessity and perhaps more importantly of such a desirability, the sections reflect the individual contributor's flavour and touch.

I am particularly thankful to Prof. K.K. Sharma, Prof. Neena Bhattacharya and Dr. Pratibha Gupta, all from University College of Medical Sciences, Delhi, and Prof. S. Dua-Sharma from M.S.R. Medical College, Bangalore, who have devoted considerable time and effort in going through the manuscripts. The help of Prof. A.S. Paintal in preparing the section on Cardiovascular and Respiratory Physiology is gratefully acknowledged. Also, sincere thanks are due to Mr. N.K. Sabharwal and Mr. S. Arora for the secretarial help.

It is hoped that the monograph would adequately reflect the advances that have been made in the particular area and bring out their relevance – basic, applied and clinical, to the national scene, and to the physiological thought in general.

K.N. SHARMA

SENSORY PHYSIOLOGY

K.K. SHARMA[1], S. DUA-SHARMA[2] and NEENA BHATTACHARYA[3]

The history of modern sensory physiology in India spans well over four decades and begins essentially with the pioneering work of Prof. A.S. Paintal and which led Heymans & Neil to talk of the works before Paintal's contributions as 'Pre-Paintal Era' (Heymans & Neil 1958). Since then a number of laboratories have come up in the country and are engaged in studying the effects of peripheral receptor systems in the physiology of cardiovascular, bronchopulmonary, gastro-intestinal and musculo-skeletal systems. In addition, considerable work has been conducted in peripheral pain mechanisms, neuropathic changes and muscle receptors in pathophysiological states such as high altitude, diabetes mellitus, haemorrhagic shock, leprosy and autonomic neuropathy. Techniques developed to excite the otherwise silent physiologically active peripheral receptors by chemicals such as histamine, bradykinin, serotonin, prostaglandins, phenyl diaguanide and to establish electrophysiological characteristics of these receptors have helped a great deal in unfolding the physiological basis of a number of sensory phenomena. Some of the major laboratories specially engaged in the study of sensory physiology are Departments of Physiology of Vallabhbhai Patel Chest Institute, Delhi; All India Institute of Medical Sciences, New Delhi; University College of Medical Sciences, Delhi; Christian Medical College, Vellore; Defence Institute of Physiology and Allied Sciences, Delhi; St. John's Medical College, Bangalore; University College of Science, Calcutta; Neurobiology Laboratory, Osmania University, Hyderabad and Departments of Biology and Molecular Biology, Tata Institute of Fundamental Research, Bombay.

PULMONARY RECEPTORS

Paintal described for the first time specific pulmonary deflation receptors (Paintal 1954, 1955a) which were termed as J-receptors primarily due to their location in the interstitial alveolar space near pulmonary capillaries and were, therefore, named as Juxta-pulmonary capillary receptors. It was reported that J-receptors were stimulated by pulmonary congestion (Paintal 1957) which may be occurring due to a rise in pulmonary artery pressure (Paintal 1969, 1970). A J-reflex was postulated, the reflex effects being inhibition of somatic muscles along with dyspnoea (Anand & Paintal 1980). The clearest demonstration of J-reflex was provided by individuals who had inhaled methyl isocyanate during the Bhopal gas tragedy in 1984 and thereafter developed

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muscle weakness as a result of marked stimulation of J-receptors that had occurred due to interstitial oedema (Paintal 1986). This understanding of muscle weakness in subjects of Bhopal gas tragedy helped in directing the correct therapy to these individuals (Paintal 1989).

While it has been observed earlier that J-receptors produce dyspoenic sensation (Paintal 1970), it has now begun to emerge that J-receptors produce dry cough (Paintal 1977a, 1986, 1989) and other effects such as bronchoconstriction and increase in blood flow (Paintal & Ravi 1980, Paintal 1982, 1983, Paintal & Anand 1992, Anand *et al.* 1993), and play an important role in high altitude pulmonary oedema (HAPO) (Paintal 1989).

An important observation in sensory receptor physiology was the use of histamine to reveal the presence of subthreshold activity in certain sensory receptors, such as pulmonary J-receptor, pulmonary stretch receptors and the slowly adapting type 1 (SA1) cutaneous receptors (Anand & Paintal 1988). For details of these receptors and their reflex effects reader is advised to go through the *Section on Cardiovascular and Respiratory Physiology*, published in this monograph.

VISCERAL RECEPTOR MECHANISMS IN CARDIO-RESPIRATORY RESPONSES

Paintal and his colleagues have worked extensively on visceral receptor mechanisms, which are described elsewhere in this monograph. Besides describing the pressure receptors in atria (Paintal 1955b) and mechanoreceptors in coronary arteries (Paintal 1972) and their role in influencing cardiovascular dynamics, the role of arterial chemoreceptors sensitive to hypotension and producing reflex rise in blood pressure has also been demonstrated (Paintal 1977b, Anand & Paintal 1990). It has been further shown that lowering the temperature greatly reduces the responses of aortic chemoreceptors to hypoxia (Paintal 1967).

Investigations of Koley and co-workers revealed the property of sympathetic fibres with aortic endings and their receptors which are involved in the homeostatic control of blood pressure (Koley 1985, Koley *et al.* 1985a,b,c). Inspired by these studies Koley *et al.* (1988a) also investigated the effect of cardiovascular reflexes in stress and role of sympathetic mechanism in such responses. These studies included electrophysiological properties of sympathetic receptors of visceral organs, and mode of working of autonomic nerves and reflexes in accomplishing different cardiovascular effects as obtained when these visceral receptors are manipulated.

Initial observations of Sherrington (1899) that distension of urinary bladder produced hypertensive effect were further studied first by Mukherjee (1957a,b) and then explored in detail to find out the possible peripheral receptor mechanisms in this reflex (Koley 1960, Mukherjee & Koley 1960, Koley & Mukherjee 1972). In a separate study Shukla *et al.* (1985) also reported similar results.

Studying autonomic responses, particularly cardiovascular and respiratory parameters, Sharma and co-workers (Shankar *et al.* 1993) found that receptors are not only present inside the urinary bladder but are also present on the urinary bladder serosal surface since topical application of a number of chemicals such as ammonium oxalate, potassium chloride, citric acid, ammonium chloride, oxalic acid, sodium hydroxide and bradykinin in the anaesthetized dogs resulted in an increase in heart rate. blood pressure and increase both in the rate and depth of respiration. By contrast, mucosal application of these chemicals did not bring about any significant change. The cardio-respiratory responses obtained were completely abolished on serosal application of procaine, section of the hypogastric nerves or by spinalectomy at T8. Bilateral cervical vagotomy and pelvic nerve section did not modify the responses. These receptors have been postulated as irritant receptors since the chemicals eliciting the reflex are irritants not specific to any pH or osmolarity. As the blood pressure responses were abolished by the administration of tolazoline hydrochloride it indicates a major role of sympathetics in such nociceptive reflexes.

A species difference also seems to exist. While dog and cat show predominently pressor responses acting mainly through sympathetic afferents, the reflex responses in rats to serosal application of the above chemicals seem to be mainly inhibitory and the major afferent pathway travels via vagus (Radhakrishan *et al.* 1985). In rabbits (Shankar, personal communication) application of these chemicals produced an occasional bradycardia. fall in blood pressure and inhibition of respiration.

In an extension of these studies to gastro-intestinal tract, similar peripheral chemoreceptors were identified on gut serosa and their reflex pathways have also been described (Shankar *et al.* 1987, Radhakrishnan *et al.* 1985). It seems that the major afferent pathway for the reflexes from the gut pass via splanchnic nerves. Receptors in the intestine which affect cardiovascular activity have also been reported by Anand (1979).

ALIMENTARY RECEPTORS AND FOOD INTAKE REGULATION

Sharma and co-workers have particularly contributed to the understanding of the role of impulses from gastrointestinal receptors in feeding behaviour and regulation of nutritional state (See also the *Section on Nutrition*, in this monograph). This group of workers have characterised various factors that influence excitability of receptors from stomach (Sharma *et al.* 1961, 1963, 1972, Dua-Sharma *et al.* 1973, Sharma 1967a, Radhakrishnan *et al.* 1986, Radhakrishnan & Sharma 1986) and intestine, mesenteric nerves and vagal afferent fibres (Sharma & Nasset 1962, Sharma 1967b, Sharma *et al.* 1972, Radhakrishnan & Sharma 1988). They have also highlighted the role of gastric chemoceptive neurons in the brain stem of frog (Ramakrishna & Sharma 1975, 1978) and showed that the operation of modulating influences on alimentary receptors act at different levels of neuraxis (Sharma 1992).

It was reported that gastric afferent discharge, analysed under varying conditions

of nutrition and under coupling effects of electrical, chemical and distension stimuli applied locally, in distant parts of the gastrointestinal tract or systemic, reveal distinguishing features related to the nature and locus of the stimulus and the spatio-temporal characteristics of the preparation (Sharma 1967a, Sharma 1967b, Sharma 1972). The modulating influences operate through a dual centrifugal control system, facilitation being routed through sympathetics, and inhibition through vagal fibres (Sharma *et al.* 1972).

A similar organisational pattern appears to be operating at the oral level, in which coupling effects of electrical stimulation and gastric distension on the gustatory receptor potential in Type I (Surfeit) and Type II (Chronic food-deprived) animals reveal differentiating features (Sharma & Doss 1973, Sharma *et al.* 1977). In Type I animals, distention decreases the rate of rise and amplitude of gustatory receptor potentials induced by electrical pulse. Cervical sympathectomy does not influence this inhibition but gastric vagotomy releases the inhibition and restores the receptor excitability. In Type II animals, distention facilitates rather than inhibits the receptor potential, and such facilitation is brought about via sympathetic fibres. Direct electrical stimulation confirmed these results in that cervical sympathetic stimulation facilitated and gastric vagal stimulation inhibited the gustatory receptor potentials.

It has been further demonstrated that stimuli applied at oral and gastric level interact and are reflected in the neuronal discharge pattern at brainstem level (Ramakrishna & Sharma 1975). In this analysis, besides 'across – neuron pattern', spatio-temporal cues play an important role in conveying the quality message. Over-all height of this pattern seems to indicate the intensity of the test material. The fact that the gastric chemoceptive afferents project to the areas of brainstem implicated in gustatory responses provides a strong base to explain the behavioural gustatory responses linked to electrophysiological parameters. Electrical recording from hypothalamic level in rats also reveals dynamic interactions amongst VMH and LH neuronal units influenced by oro-gastric inputs and the state of nutrition (Sharma *et al.* 1979). Still higher up, the internal and external cues acting as sources of peripheral inputs through these receptor systems have been shown to bring about appropriate behavioural feeding responses through interaction with hypothalamus-limbic-sensorimotor cortical neuronal circuits (Kravtsov *et al.* 1991, Sharma 1992). Parallel studies on olfactory receptors have also shown centrifugal control as being involved in such modulations (Pager 1977). These studies clearly demonstrate that the change in the nutritional state (e.g. Type I Vs. Type II) and reflected in the microenvironment, modulates the receptor characteristics in a manner that there is not only a quantitative but qualitative change in the registration of and response to application of identical stimuli. The flow of information from these receptors to the brain is not all in one direction. 'Tuning' of the receptors through the centrifugal controls via short and long feedback loops (Sharma *et al.* 1972) allows sensory pathways to act as variable filters so that stimuli tagged with a particular attribute or feature are alone allowed for detailed analysis. By such means, it is possible to attenuate or amplify afferent signals or switch 'on' or 'off' the inputs, thereby selecting a particular input at a particular time (Sharma 1992).

Sharma's group have also investigated the role of taste and other sensory qualities of diet, caloric intake and food deprivation (Jacobs & Sharma 1969, Dua-Sharma *et al.* 1973, Radhakrishnan & Sharma 1986, Radhakrishnan *et al.* 1986) and cross-cultural biases in the regulation of feeding behaviour, food preferences and food habits (Moskowitz *et al.* 1975, 1976, Sharma *et al.* 1979). For instance, it was shown that selective gastric vagotomy significantly reduced the intake of sweet substances such as sucrose, glucose and saccharin, the maximum suppression being for 5% sucrose, a moderate suppression for 1% and 0.5% and no significant change in the intake of 0.1% sucrose. The results also indicated a probable reduction in the ability of these vagotomised rats to discriminate taste intensities within a close range (Radhakrishnan *et al.* 1986). In another series of experiments, it was observed that naloxone produced a significant reduction in the intake of sucrose, glucose, saccharin, sodium chloride and water in sham-vagotomised rats but a suppression of only sucrose in vagotomised rats. The differential effect of naloxone in intact and vagotomised rats suggests a possible involvement of endogenous opioid mechanisms in the gastro-gustatory interactions in taste. The selective reduction in the preference for sapid substances could be one of the mechamisms by which naloxone suppresses food intake in intact animals (Radhakrishnan & Sharma 1986). Later, Bhatia *et al.* (1981) investigated the taste sensitivity to phenylthiocarbamide (PTC) and gustatory response to glucose during different phases of menstrual cycle in female subjects and found maximum pleasantness peak at 1.0M glucose solution in all phases of menstrual cycle while pleasantness scores were higher during ovulatory phase. The PTC responses were dynamic and showed a shift from non-tasters to tasters during ovulatory phase. It is likely that gustatory receptor activity is modulated as much by circulating hormones as by other factors like gastro-gustatory receptor interactions.

Other workers investigating the role of peripheral mechanisms/receptors in the control of satiation of hunger and thirst have contributed to the understanding of these mechanisms by their studies on gastric stretch receptors (Paintal 1953, 1973) and intestinal chemoreceptors (Sharma & Nasset 1962). The role of these gut afferents in regulation of activity of brain regions concerned in food intake has clearly been demonstrated (Sharma *et al.* 1961, Mohan Kumar 1971).

GENITAL RECEPTORS AND SEXUAL BEHAVIOUR

Dua-Sharma and colleagues have conducted a series of studies investigating systematic exploration of neural substrates involved in sexual behaviour (Dua-Sharma and McLean 1964) and have clearly brought out the important role of genital afferents in sexual arousal and other overt forms of sexual behaviour (Dua-Sharma *et al.* 1977). While stimulation of well-defined, discrete areas in the brain lead to penile erection, quasipruritic scratching of genital area, seminal discharge with motile sperms, grooming, pelvic thrusting and other overt forms of sexual behaviour, these nodal brain regions have been shown to be markedly influenced by stimulation of genital receptors. It seems that on one hand these central nervous structures have an important role in maintaining the functional integrity of genital receptors, on the other hand the evidences

strongly suggest the existence of both hormonal and sensory feedback from the genital receptors to characterise the activity of these central nervous regions. The responsiveness of hypothalamic and mesencephalic neurons to vaginal stimulation varies according to the hormonal profile (Chhina *et al.* 1968) and the differential changes can be recorded from genito-testicular afferents (Dua-Sharma *et al.* 1974).

Sectioning of the nervous dorsalis penis brought about a marked decrease in the number and functioning of the genital receptors, particularly conical projecting variety. Testes also showed marked decrease in alkaline phosphatase, cholinesterase and PAS activity after such sectioning (Kanaka & Dua-Sharma 1974). It has been suggested that testicular activity, among other factors, is influenced by feedback influences from genital receptors, and in which role of nervous dorsalis penis is important. More recently Mallicki *et al.* (1994) have demonstrated that stimulation of dorsal penile nerve of the rat evokes field potentials in the hypothalamic medial preoptic area and affects its single and multi-unit activity. The resultant sexual activity would thus be linked to the status and integrity of genital receptors and the multilevel analysis taking place at local receptor sites, gonadal levels and various levels of neuraxis.

NOCICEPTORS AND PAIN

Taking lead from earlier observations on formalin-induced pain in rodents and cat (Dubuisson and Dennis 1977) which produces two phases of pain responses — an early phase of direct chemical stimulation of peripheral nociceptors and late phase involving inflammation, Nayar and co-workers developed a tonic pain model in monkey (Alreja *et al.* 1984) and studied the peripheral and central mechanisms of stress induced analgesia (Alreja *et al.* 1985, Nayar *et al.* 1988). Other workers using models of inflammatory pain due to 5-HT (Kulkarni *et al.* 1985) and acetic acid-induced peritoneal irritation (Sharma & Singla 1984) in mice concluded that peripheral nociceptor sensitivity is modified by catecholaminergic mechanism, presumably alpha and dopamine receptors acting in the peripheral pain sensory pathways besides central nervous system. Kanaka (1988) reported that nociceptors activated by algesic chemical substances can modulate the profile of the non-nociceptive afferents like deep pressure. The possibility of such interaction and inhibitory modulation being peripheral in locus was convincingly put forward. Further, the animals developed a state of hyperalgesia as age advanced and it was brought out that peripheral inputs may play a role in bringing about this hyperalgesic response (Kanaka *et al.* 1989). Shahni and colleagues by their experiments using high voltage/frequency electrical stimulation to relieve pain in human volunteers described the role of afferent inputs from a relatively large diameter sensory fibres and the "alpha neuronal pool" excitability in the antinociception during electrical stimulation (Shahni 1966, 1982, Shahni & Capadia 1986). The fact that central neural mechanisms have a dual differential control — facilitatory and inhibitory, on nociceptive afferents is well known. Bhattacharya & Sharma (1986) have demonstrated the facilitatory role of cortex on reactions to painful stimuli. Removal of discrete neural regions above the midbrain level resulted in increased latent period of the nociceptive reflex indicating increased pain threshold. It seems that basically cerebral cortex either exerts an inhibitory

control over the endogeneous analegesia system (EAS) or a facilitatory influence on the facilitatory regions thereby influencing the peripheral nociceptive inputs (Bhattacharya & Sharma 1988). Extension of such studies to human work by using Polyelectroneurographic technique (PENG) and event-related PENG records to analyse true system functions have revealed difference in EEG and ISEP (infraslow electrical process) maximum cross correlation function means between pre- and post-acupuncture recordings, as well as between pain patients and healthy subjects (Bhattacharya *et al.* 1991, Sharma *et al.* 1994). If further elucidated, PENG could serve as a potential powerful non-invasive tool for diagnostic and therapeutic measures in clinical neurophyisology.

Investigating the role of sympathetic afferents in experimental cardiac ischaemic pain in cats, Koley *et al.* (1985d, 1988b, 1989) have shown that sympathetic afferents of A delta and C fibres convey different sensations from the ventricle, pericardium, epicardium, from the wall of the coronary vessels and wall of the aorta. It was also shown by them that sympathetic afferents of A delta and C fibres can participate in conveying ischemic pain sensation from the heart to the CNS. Myocardial ischemia is accompanied by formation of lactic acid, bradykinin and prostaglandins.

Reflex regulation of muscle atrophy in chronic pain

Swami and co-workers experimenting with frog gastrocnemius muscle after inducing muscle atrophy by sectioning of the sciatic nerve examined the role of peripheral sensors in skeletal muscles which are sensitive to external cathodal electrical fields applied to denervated muscles. This cathodal electrical field retarded the process of muscle atrophy, whereas external anodal field hastened the atrophy (Krishnamoorthy & Swami 1954, Bojji & Swami 1971). These workers also noted that the muscle enzymes involved in energy production possess positive electrical charge in contrast to the degradative enzymes having negative electrical charge. It was observed that protein synthesis in denervated muscle could be increased by cathodal fields as is in normal muscles (Sreelakshmi & Swami 1972). Investigating the mechanism of muscle atrophy during acute inflammation in painful joints in experimental animals, Krishna Reddy and co-workers found the critical role of peripheral nociceptors in muscle degeneration (Krishna Reddy 1980, 1985, Krishna Reddy *et al.* 1989) since transection of somatic nerve supplying the muscle by elimination of neural activation reduced the typical reflex atrophy.

PERIPHERAL NERVES IN DISEASE

Dastur and co-workers have investigated the relationship between patterns of nerves distributed in a region and the sensation contributed by that region in different disease conditions like leprosy (Dastur 1955), lathyrism (Dastur 1962), manganese poisoning (Dastur *et al.* 1963, 1969) and ageing (Dastur 1985) and observed marked changes in cutaneous sensibiltiy. Misra and co-workers (1985) in separate studies reported on auditory nerve conduction and

reflexes in workers spraying pesticides and found a variety of biochemical and clinical changes.

Antia and co-workers (Antia *et al.* 1975, Shetty *et al.* 1977, Jacobs *et al.* 1987) studied teased fibres and tissue culture preparations to examine cutaneous nerves in leprosy patients. Immunohistological, ultrastructural and other methods were also employed. Their studies indicated lipids or lipoprotein receptors on the membrane of Schwann cells of peripheral nerves as routes of entry of bacterium *M. leprae* (Mukherjee *et al.* 1980).

Changes in peripheral nerve conduction that occur during stress of high altitude, diabetes melitus and haemorrhagic shock in man were investigated by Malhotra, Selvamurthy and Lazar Mathew. Peripheral changes were compared with evidence of central neuropathy as seen in diabetes mellitus and long-term adaptation in high altitude (Malhotra *et al.* 1976, Mathew *et al.* 1977, Selvamurthy *et al.* 1981, 1983, Selvamurthy 1984, 1988). These studies revealed the significance of monitoring spontaneous and evoked activity in peripheral and central neurones in any stressful condition as an index of health of the organism.

SENSORY ENDINGS IN INTERPHALANGEAL JOINTS

In a series of studies Devanandan and his co-workers investigated muscles, nerves and sensory receptors of the joints of the hand in Bonnet monkey (Devanandan *et al.* 1980, 1983, Devanandan & Babu 1989). They have shown that encapsulated endings are situated exclusively in the lateral and ventral aspects of the joint capsules which are capable of monitoring transient joint movements. They have also contributed to the understanding of weight perception in the hand of normal subjects and in patients with leprous neuropathy (Victor Raj *et al.* 1985).

They also studied sensations originating from passive movement of proximal interphalangeal joint of the index finger in humans (Babu & Devanandan 1989). Studies were carried out after anaesthetising different nerves of the finger. Results indicate that (i) sensation of rapid movements is less affected by the absence of afferents from one or two regions, (ii) digital afferents affect the threshold of perception and (iii) directional sense is seen to be associated with the lumbrical muscle.

In recent years these studies have been extended to investigate the central projections of these phalangeal muscle and joint afferents by conducting meticulous histochemical and electrophysiological studies (Thangam *et al.* 1989).

INVERTEBRATE RECEPTOR PHYSIOLOGY

Ramakrishna, based on his studies on arachnids, concluded that in the median eye of scorpion, the outer segment of the sensory receptor cell acts as a current sink while the cell body acts as a source during exposure to light. The influence of the CNS on

the sensory cells is greater on 'b' wave of its electroretinogram than on the 'c' wave (Ramakrishna 1977, 1983, Ramakrishna & Pampapathi Rao 1970). Rodriques and her colleagues have identified in different mutants of *Drosophila melanogaster* the gustatory receptors of sugar neurons, the gene involved in regulation of neurons of olfactory pathways and odour coding and the distribution patterns of olfactory sensory structures, antennae, maxillary pulp, gustatory sensillae located in the legs and mouth parts and larval sensillae (Rodrigues 1980, Rodrigues & Siddiqui 1978). The electrical responses of taste receptors of x-linked gene mutants of *Drosophila* defective in pyranose receptors, chemosensory dendrites of labellar taste bristles and axonal counts of prominent nerves of mouth were also described by them (Rodrigues & Siddiqui 1981, Rodrigues & Buchner 1984). A new type of compound, sensillum, was observed in labial organ by Singh & colleagues (Nayak & Singh 1983). The primary sensory projections from sensillae of antenna and maxillary pulp were found to converge in the lobes of the brain. Seven types of sensory fibres were observed in the projection from labellar sensillae to the brain called suboesophageal ganglion (Venkatesh & Singh 1984, Singh & Nayak 1985).

FUTURE LEADS

Sensory receptor physiology has emerged as an outstanding development in keeping with the astonishing progress in the technology of molecular biology and provides a basis for the understanding of intimate mechanisms operating at cellular, sub-cellular and biomolecular levels. The need appears to interface this knowledge with organ-systems and the organism as a whole wherein lies the potential for future direction of research. Information emerging from reductive sciences (e.g. molecular biology, cell biophysics) should be put together in a manner that appropriate function at organismal level ensues.

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NEUROPHYSIOLOGY AND BEHAVIOUR

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With the ushering in of the independence in the country, could perhaps be labelled the beginning of neurosciences, and neurophysiology in particular. Names of persons like B.B. Dikshit, Baldev Singh, B.K. Anand, B. Ramamurthi and Brahmayya Sastry come to the forefront. With the epoch-making discovery of the 'Feeding Centre' by Prof. B.K. Anand along with John Brobeck of Philadelphia in 1951, already the ground work had been laid for placing India in the world scientific map and recognise legitimate development of neurophysiology in the country at global level. By a happy coincidence, while Anand got basically involved in exploring central neural organisation of feeding behaviour, Paintal had entrenched himself in unravelling several facets of sensory receptor systems not hitherto known. Thus search for information-flow from periphery to centre and in the reverse direction, was already on without perhaps realising the potential significance for the future trends.

In the early fiftees, B.K. Anand established the first Neurophysiology Research Unit (ICMR) at Lady Hardinge Medical College, which was later shifted to All India Institute of Medical Sciences. Hypothalamus, then known as the Head Ganglion of the Autonomic Nervous System, had become the hub of activity and virtually every conceivable aspect of its functioning was being explored. Stereotaxic stimulation, ablation and recording from deeper regions of brain were the major approaches to study the control and regulation of food and water intake, and of cardiorespiratory, gastrointestinal, reproductive, hormonal and several other autonomic and visceral functions. In all these investigations a running theme seemed to be localisation of 'centres', concept of hiearchical levels and operation of reflexes. Under the dynamic leadership of Prof. B.K. Anand were nurtured a number of young scientists like S. Dua-Sharma, G.S. Chhina, K.N. Sharma, S.K. Manchanda, T. Desiraju, Usha Nayar, Mohan Kumar to name a few and who later on became names of their own in the field of neurophysiology at global level. Today quite a few major centres spread out in the country exist which are substantially contributing to neurophysiological research; and these include All India Institute of Medical Sciences, Vallabhbhai Patel Chest Institute and University College of Medical Sciences, all in Delhi; St. John's Medical College, M.S. Ramaiah Medical College and National Institute of Mental Health & Neuro Sciences, all in Bangalore; Goa Medical College; Institute of Neurology and P.G. Institute of Basic Medical Sciences, Madras; CMC, Vellore; Post Graduate Institute of Basic Medical Sciences and University College of Science, Calcutta; and Institute of Medical Sciences, Banaras Hindu University, Varanasi.

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The following description is neither a review nor an exhaustive coverage but gives a glimpse of some of the better-known works that have attracted worldwide attention, and form the major direction of research efforts in neurophysiology in the country.

FEEDING BEHAVIOUR

With the discovery of 'feeding' and 'satiety' centres in rat by Anand and Brobeck (1951) two opposing mechanisms in the hypothalamus were postulated that regulate food intake. That similar centres also existed in other species like cats and monkeys were convincingly demonstrated by Anand and his colleagues (Anand *et al.* 1955). It was suggested that feeding behaviour is probably based on feeding reflexes operating through the spinal cord and brainstem levels (Brobeck 1960). These reflexes are facilitated by the feeding centre and inhibited from the satiety centre, and the activities of these hypothalamic regions provide the basis for hunger and satiety states (Anand 1967). As a result of feeding, certain changes are produced in the body which stimulate the activity of satiety centre, which in turn suppresses the activity of feeding centre and brings about the state of satiety. Subsequently when the food eaten is disposed of as heat, work done or stored energy, the activation of satiety centre is removed and the feeding centre activity becomes prepotent leading to the state of hunger (Anand 1962, 1963). These hypothalamic centres are further influenced from the limbic system of the brain to provide discriminative appetite (Anand 1961).

Working on the possible mechanism of hypothalamic control Anand and his colleagues in a series of studies confirmed that hypothalamus contains elements sensitive to 'qualities' of circulating blood and among which availability or utilisation of glucose seems to be an important signal. Electrical activity of hypothalamic feeding and satiety centres clearly indicated that hyperglycaemia, produced by intravenous infusion, increased activity in satiety centre with a concomitant drop in feeding centre activity. Conversely hypoglycaemia produced by insulin slowed the activity selectively in the satiety centre (Anand *et al.* 1961). Electrical activity of single neuron in hypothalamic feeding and satiety centres further confirmed these observations and showed a more close correlation of spike activity with magnitude of arteriovenous glucose difference (glucose utilisation in the body) than with the arterial blood glucose level (Anand *et al.* 1964). Thus while the need for glucose homeostasis being the primary motivating drive located in the hypothalamus was emphasized, the general design did allow the exercise of modulatory influences from other metabolic and non-metabolic sources including the gastrointestinal tract (Sharma *et al.* 1961). This was Anand's decade of research on Brain and Feeding Behaviour which catalyzed an immense amount of research effort all over the world.

Sharma continued his interest in the role of various inputs into the feeding centres emanating from the GIT under various states of perfusion by exploring the electrical activity of the mesenteric nerves presuming that the nutrients perfusing the gut lumen may have a faster system of sending information (Sharma & Nasset 1962). He expanded this work and described the electrophysiological characteristics of various types of receptors present in the alimentary tract and the functional role played by these receptors

in the regulation of food intake (Sharma 1967a,b). With further progress of work the importance of oro-gastric and brainstem interactions in food intake, the differential modulating control of alimentary receptor mechanisms and the behavioural analogues in animals and humans laid a strong foundation for examining the dynamics of the system and neuronal networks rather than restrict the view to 'centres'. Sharma ranks amongst the few most prominent workers who have developed this concept and has suggested a multistage organisation of the motivational behaviour like feeding in which at the very first step the oro-sensory determinants are processed for afferent synthesis in linkage to the dominant homeostatic need and environmental and experiential factors to guide the behaviour of the organism. The scheme of neural networks of connections between fasciculus solitarius and oro-gastric receptor systems with a possible biasing by the available energy-pool as put forward by him is bold, rational and comprehensive for the sensory mechanisms (Sharma *et al.* 1979, Sharma 1992). But at the level of information processing and synthesis in the CNS for sending command signals for behavioural output there is need for designing other networks involving various CNS structures, e.g. hypothalamus, striatal areas and limbic system which are known to play a role in the regulation of feeding behaviour (Oomura *et al.* 1992).

While the Sharma group investigated various types of sensory mechanisms including those initiated by the GIT with relevance to regulation of food intake (also see *Section on Sensory Physiology* in this monograph, Manchanda and colleagues of the AIIMS group concentrated on the motor aspects. Manchanda had earlier shown that well-organized mastication and swallowing can be obtained by the stimulation of lateral hypothalamus (Manchanda 1965). It was further demonstrated that the electrical stimulation of LHA feeding centre in conscious animals not only elicited stimulus-bound feeding but also produced changes in gastric motility depending on the initial state of gastric activity and according to a pattern expected during and after feeding (Glavcheva *et al.* 1972). In another study they demonstrated the role of cerebellum in the regulation of gastric motility (Manchanda *et al.* 1972).

It is now an acceptable hypothesis that sensory activity of foods and their consequent appraisal is a critical determinant of innate as also of acquired feeding responses ensuring an oral selection and metering of intakes. The appraisal will include its taste, flavour, texture, viscosity, volume, temperature and perhaps other physicochemical characteristics. These chemosensory signals from food in effect provide a hedonic matrix that determines food acceptance, choice and intake. The gastrointestinal signals which constitute both slow- and fast-acting sensory system share the CNS organizational characteristics with the oral sensory system. At the postabsorptive and systemic level, food as a nutrient acts as a metabolic signal on regulatory centres and through positive and negative feedbacks initiates modulation of the ingestive processes (Sharma *et al.* 1975, 1977, 1979).

The animal experimental models hitherto mentioned are applicable to human beings too for well-planned studies on humans have indicated that nutritional background,

previous dietetic history and external environmental stimuli interact in such a way that the prepotent sensory properties of food and experiential factors subserve to bring about relevant metabolic adaptive changes, taste preferences and food habits (Moskowitz *et al.* 1975, 1976). Such studies may be of significant interest to the nutritionist, food and flavour chemist and even the market researcher and food manufacturer.

Exploration into the ontogenic aspects of neural regulation of food intake in India is relatively recent. It has been known for some time that whereas the connections of some neurons are genetically established, those of some others are dependent on sensory stimulation during early development. Will the experiences of the fetus determine the sensitivities and preferences of the adult as far as the regulation of food intake is concerned? The question was tackled by Jacobs and Sharma in 1969 (Jacobs & Sharma 1969) who reported that the maturation of gustatory apparatus in the rat is complete by the day 14 of neonatal life and concluded that for nutrition the neonate is primarily dependent on taste cues and not for calories. Sharma in a subsequent publication (Sharma 1975) again emphasised the nature and early development of the oral detector system in the neonate and its relevance to nutrition in the newborn human who too will suck/eat for taste rather than calories. The AIIMS group, particularly Mathur, Nayar and Manchanda who published a series of papers in this field, subscribed to the idea that the most basic neural mechanisms regulating intake develop first and those for fine-tuning develop subsequently. They described the steps of development of electrical activity of LHA and VMH activity. The development of sensitivity to glucose in hypothalamus precedes the behavioural response to hyperglycaemia which occurs well after weaning (Mathur *et al.* 1983, 1986, 1992).

CENTRAL CARDIOVASCULAR CONTROL

Exploring the central neural mechanisms underlying visceral functions, Anand and his colleagues undertook a series of studies and showed a variety of changes in visceral and metabolic activities on stimulation and/or ablation of hypothalamic – limbic – forebrain regions (Anand 1970). While working on neural control of cardiovascular system, Manchanda gave a new thrust to these studies (Manchanda *et al.* 1974, 1975) and put forward the view that capsular approach of having well-demarcated cardiovascular centres is rather questionable and inadequate to explain the comprehensive repertoire of regulatory controls available to the brain. A systems approach was advocated to explain various visceral regulations (Manchanda 1970a,b).

Srimal and co-workers demonstrated cholinergic involvement in the mediation of pressor as well as depressor responses to drugs when applied on the vasoactive area on the ventral surface of medulla (Srimal 1985, Raghubir *et al.* 1981). The muscarinic cholinoceptors were observed to have an inhibitory action, whereas nicotinic cholinoceptors at the hypothalamic, medullary and spinal levels played a facilitatory role (Bhargava 1976). It seems that alpha adrenoceptors play an inhibitory role at medullary level and beta receptors an excitatory role at the hypothalamic level in the central cardiovascular control in cats (Bhargava *et al.* 1978). It has been further shown

that catecholaminergic receptors present in nucleus raphe dorsalis appear to influence sympathetic preganglionic neurons in the intermediolateral columns of the spinal cord which modulate activity of heart and blood vessels (Saxena *et al.* 1985), whereas cholinergic compounds were observed to have opposite effects (Saxena *et al.* 1983).

Gogate, Dhume and colleagues (Dhume *et al.* 1975) demonstrated the frequency modulation effect of hippocampal stimulation on cardiorespiratory responses and found functional dissociation within hippocampus related to visceral and behavioural patterns (Dhume *et al.* 1976). The controversy on whether it is feasible to volitionally condition heart rate slowing (a visceral regulation) without involving reflexes created by somatic muscular manipulation, appears to have been resolved by demonstrating that such conditioning is feasible (Bindu & Desiraju 1988).

AFFECTIVE BEHAVIOUR AND AGGRESSION

Like many other behavioural studies, pioneering efforts to study the neural basis of affective behaviour too were made by Anand, Dua and Chhina (Anand *et al.* 1957a,b, 1959a). The "limbic system", as it came to be designated, was considered to have over-riding controlling influences on behavioural tasks which were basic to homeostasis and survival as common denominators over a wide range of functions, e.g. consummatory behaviour like ingestion of nutrients, sexual play including copulation, defence and aggression and of course the pleasure, gratification and affective display that accompanies these responses. To further establish the primacy of limbic system in the elaboration of these innate behaviours, Anand *et al.* (1959b) showed by electrophysiological techniques that the phylogenetically older parts of cerebellum which bring about sensori-motor coordination and affect visceral functions,i.e. paleo and archicerebellum, have profuse connections with the phylogenetically older limbic system. More recently Mascarenhas et al (1978) have shown that stimulation of hypothalamus produces a well defined attack response which can be attenuated by simultaneous stimulation of caudate nucleus. Particular attention has since been paid to clarify the neural and neurochemical mechanisms involved in the elaboration of defence and flight behaviours and predatory aggression as distinct from affective attack. It is now established that the basic pathways starting from hypothalamus are essentially cholinergic but are markedly influenced by adrenergic and opioidergic connections at the level of substantia nigra, periaqueductal gray and tegmental areas (Dawra *et al.* 1988a,b, Saha *et al.* 1993a,b). It is also possible to produce self-aggression by manipulating the dopaminergic and adrenergic pathways. Treatment of CNS with opioids inhibits self aggression but naloxone enhances it. Therefore pain, self-aggression and affective display may have a mechanismal link (Sharma *et al.* 1991).

BRAIN DEVELOPMENT

Studies on the sequential development and maturation of neurons of the spinal cord (Rizvi 1986), cerebellum (Hasan & Abdi 1988), hippocampus, lateral geniculate

body (Damayanti *et al.* 1983) and visual cortex (Masood *et al.* 1988) have been carried out in human and mammalian embryonic and foetal brains in several laboratories of the country to find out both the anatomical and physiological development of various brain regions. Most of these studies have been devoted to investigating the effect of malnutrition, undernutrition and hormonal changes on the development of brain.

Bijlani and co-workers demonstrated a reduction in cerebellar surface with prolonged mitosis and proliferative activity in the external granular layer in undernourished rats. These changes were shown to be due to prolongation of S1 phase and shortening of G2 phase of mitosis, with consequent delay in cell migration into the external granular layer of the cerebellum (Deo *et al.* 1975, Gopinath *et al.* 1976). Gopinath and her colleagues while investigating the effect of malnutrition on the organization of spinal cord and proliferation and maturation of cerebral cortex and cerebellum (Chowdhary *et al.* 1982, Gopinath 1984) showed deficient development of these structures in the malnourished subjects.

Desiraju and his colleagues in their studies on the effect of malnutrition on the development of brain using anatomical, physiological and biochemical techniques showed that dendritic growth and branching, though slower in undernourished rat pups, were greater than that seen in normal animals (Gundappa & Desiraju 1988). They also demonstrated that learning abilities of the undernourished animals were greater than that of well-fed age-matched animals (Mascarenhas *et al.* 1986). This was attributed by them to greater dendritic growth although the neuronal development was slow. These workers also studied the extent of prevention of occurrence of these aberrations by providing normal nutrition from the post-growth spurt (of brain) age and observed that it helped only to a limited extent (Gundappa & Desiraju 1988).

Investigating the factors influencing the developing brain, Manchanda, Nayar and co-workers studied the electrophysiology of cerebellum during postnatal growth of undernourished rats. They showed that undernutrition produces retardation of neuronal activity as measured by spontaneous unit activity of Purkinje cells (Puthuraya *et al.* 1980). Their subsequent studies demonstrated that neurons of rat ventromedial hypothalamus developed normal glucose sensitivity at about 21 days of age. This could be preponed to 15 days of age by administering glucose to rat pups from 5th day of age. Responses of lateral hypothalamic neurons to glucose in younger age were found to be opposite to those observed in the adult age (Mathur *et al.* 1983, 1986).

HOT WATER EPILEPSY

It is well known in South India that hot water bath over the head induces epileptic seizures in a significant patient population (Satishchandra *et al.* 1988). Ullal has developed an animal model in rat (Satischandra *et al.* 1993) resembling human hot water bath epilepsy and found the seizures to be generalised clonic type associated with generalised high-voltage spikes and polyspike activity. There appears to be kindling phenomenon associated with hyperthermia, and neuronal damage noticed in Sommer's

sector of hippocampus and part of cingulate regions. Hippocampal temperature profiles in 'seizure prone' and 'seizure resistant' rats along with population activity of the neurons accompanying hyperthermia are being worked out and indicate interesting trends. Working on mathematical modelling of neural networks and kindling of focal epilepsy Ullal has shown progressive increase in After-discharge (AD), drop in AD threshold, spontaneous AD, pulse frequency dependence of kindling rates, and even 'status epilepticus', once the system was trapped in another domain of activity (Mehta *et al.* 1993).

SLEEP, CONSCIOUSNESS AND HIGHER BRAIN FUNCTIONS

The EEG correlates of the wakeful, sleep and dreamy states of consciousness are well described in text books and monographs. Desiraju's outstanding contributions in this area are, however, worth mentioning. Initially, in collaboration with Purpura in the USA, Desiraju produced data on various excitatory and inhibitory processes gating the synaptic transmissions between lateral and medial thalamic nuclei and clarified their relationship with the inputs from basal ganglia and cerebellum (Desiraju & Purpura 1969, 1970). He then characterised the operational aspects of thalamo-cortical and cortico-cortical projections which form the basis of EEG. Electrophysiological linkages between the limbic and neocortical regions were specially described which came to be recognised as some of his most original work (Desiraju 1973a,b). He studied the patterns of alterations of electrical rhythm which occur in various brain regions during different sleep states and identified the "dynamogenic" and "hypnogenic" regions in the reticular formation and elsewhere in the brain. He has also described the characteristics of single unit impulse discharges in parietal and prefrontal cortices for all stages of sleep-awake cycle of the monkey. These studies were the earliest of its type which documented the electrophysiological interplay between the higher brain regions which are involved in mentation, i.e. thinking, imagery, planning etc. during different stages of sleep and wakefulness (Desiraju *et al.* 1966, 1967, Mancia *et al.* 1968, Desiraju 1976a,b). Desiraju also devoted time to philosophical considerations of consciousness and theorised to bring to attention those aspects of Hindu philosophy which are in consonance with advanced thinking in modern neurophysiology (Desiraju 1984). He has formulated the non-dualistic evolutionary theory of the conscious state, based on the knowledge of some of the principles of organisation of brain and its higher cerebral areas. Drawing attention to computer modelling approach in language behaviour, Narasimhan (Narsimhan 1981) argues that behaviour modes must satisfy phylogenetic continuity, physiological realisation, and be complete enough to articulate all aspects of behaviour.

A series of studies on preoptic hypothalamic region (POA) by Chhina and Mohan Kumar have revealed its involvement in several functions like sleep-wakefulness, locomotor activity, body temperature, reproduction etc. linked to different sets of neurons, connectivity and receptor types. It has been demonstrated that selective POA neurons showed differing discharge pattern associated with synchronised or desynchronised EEG activity, respectively. The amygdala and brainstem reticular

formation exerted excitatory influence, while hippocampus produced inhibitory influence on the POA neuronal discharge (Mallick *et al.* 1983, 1986, Mohan Kumar *et al.* 1984, 1985). More recently these workers have shown noradrenergic system involvement in wakefulness, paradoxical sleep and slow wave sleep and have provided evidence for the possible basis of these different conditions. Noradrenergic fibres from locus coeruleus, projecting to the thalamus and cortex, are implicated in waking, attention, cognition and other higher functions. Interaction of locus coeruleus fibres with cholinergic cells of brainstem plays a role in the genesis of paradoxical sleep. The noradrenergic fibres ascending through the ventral bundle, and terminating in the preoptic area, are involved in the genesis of sleep – probably slow wave sleep (Mohan Kumar 1993).

Applying state-of-the-art techniques Mukundan and his colleagues at NIMHANS have been studying cognitive psychophysiology and shown that Event-Related Potentials (ERPs) reflect specific processes of human information processing. One of the systematic approaches to study underlying neurophysiological mechanisms of these ERPs is the topographic mapping obtained from multichannel recording so that the activity generated by the brain in three-dimensional space and pinpointing the generators of the scalp recorded potentials using the 2- or 3-dimension dipole models, could be effectively pursued in normals and clinical population. Trends indicated age-related changes in the topography and the global field power of the attention related event components. Various clinical subgroups like dementia, psychosis and schizophrenics have shown differing changes in ERPs and brain maps. In schizophrenics there is asymmetry in distribution, showing a left deficit (Sudha Suresh 1994). The methodology developed can pinpoint source localisation and thus contribute to the localisation of deficient higher brain functions.

Another powerful tool to investigate higher brain functions in recent years has been the use of polyelectroneurography (PENG) by Sharma and his group (Bhattacharya *et al.* 1990, 1991, Sharma *et al.* 1994). PENG has the potential advantage of simultaneous recording of different brain bioelectric processes (BBP) such as EEG, infraslow electrical process (ISEP), impulse neuronal activity (INA) and DC or steady potentials (SP) from a single electrode pick-up device. It allows one to have a direct idea of various BBPs from the same as well as a number of brain sites simultaneously, and over a long period of time. It has been found applicable to such diverse conditions as sleep and wakefulness, motivations and emotional stress, nociception and pain. Analysis of event-related PENG records has been undertaken using phases of other native and parameterized processes as functional keys so that true system functions – spatio-temporal relationships, for both multiple idential and different processes could be examined.

EMERGING TRENDS

Neurophysiology in India did have its germination from several of the outstanding laboratories the world over and it has now undoubtedly achieved a status from where a virtual 'take off' is simply within sight. The twentieth century technological

accomplishments have brought in their vogue the importance of reductionist sciences, and the scope and future of physiological sciences per se, is being questioned and debated. And perhaps this dilemma is not any more apt than its linkage to neurophysiology. After all neurophysiology is basically concerned with information transfer, regulations and controls to explain the basis of behaviour – a feature of holistic dimensions. It is therefore worthwhile considering at this juncture if the research efforts in future be primarily directed towards reductionist sciences like molecular biology to explain physiology, or they should aim at 'physiology' – the study and knowledge of life, which will be necessary for an understanding of what all the molecular biology means.

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CARDIOVASCULAR AND RESPIRATORY PHYSIOLOGY

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This review of work on cardiovascular and respiratory physiology is not intended to be exhaustive but rather to provide an insight into some of the better-known studies done in India.

CARDIOVASCULAR PHYSIOLOGY

Among the noteworthy, but scattered, studies on cardiovascular physiology in India, one of the earlier studies relates to the Bainbridge reflex.

The 'Bainbridge effect'. It has been known for long that injection of fluids intravenously causes an increase in heart rate in different animals, an increase that is abolished by vagotomy. This effect, first demonstrated clearly by Bainbridge (1915), has been known as the Bainbridge reflex and has continued to be taught to medical students to this day (e.g. see Ganong 1993) as a reflex that occurs due to stimulation of sensory endings in the right atrium by injecting fluids intravenously. Pathak carried out experiments on the isolated heart and found that distension of the atrium of isolated heart caused acceleration of the heart rate, thereby showing that a reflex was not involved. This observation first made on the heart of frogs (Pathak 1958a) was later confirmed in the hearts of dogs by him (Pathak 1958b, 1959). These papers have been reviewed along with other work by Linden & Kappagoda (1982).

That several mechanisms may be involved in the 'Bainbridge effect' is revealed by the observations of P.D. Gupta who, in carefully controlled experiments on dogs, observed that infusion of blood into dogs that had received beta-receptor blockers caused tachycardia but that bradycardia occurred in dogs whose spinal cord had been sectioned at about C7 and had received acceleratory blockers. He, therefore, concluded that there was a reflex afferent pathway running in the spinal cord and an efferent pathway running in the vagi (Gupta 1975). Subsequently he extended this work to delineate more precisely the pathways, and demonstrated that the afferent pathway passes through both the ventral and dorsal roots of the sympathetic at the level of TI (Gupta & Singh 1979, Gupta 1977). It should be noted that experiments involving volume loading are viewed sceptically as it is not possible to define the precise region of the heart or blood vessels that is responsible for generating the afferent impulses: localized stimulation of specific regions have therefore been preferred (See Linden &

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Kappagoda 1982). This criticism would apply to the experiments involving a-v shunts. As shown by Gupta & Singh (1979), opening such shunts causes cardioacceleration which they believe is due to a reflex whose afferent pathways run in the vagus.

It is generally believed that stimulation of carotid chemoreceptors caused bradycardia as first shown by Comroe (1939). Gupta & Singh (1981) showed that the effect of stimulating chemoreceptors could lead to tachycardia when the initial heart rate is low. They showed that carotid chemoreceptor stimulation elicited both cardioacceleratory and cardioinhibitory reflexes. Subsequently Gupta & Singh (1987) showed that similar reflexes are elicited from carotid chemoreceptors during apnoeic asphyxia.

Bezold-Jarisch effect. The term Bezold-Jarisch effect, as pointed out by Krayer (1961), should be limited to the reflex fall in blood pressure and heart rate owing to stimulation of sensory receptors in the heart by veratridine or various mixtures of alkaloids of veratrum. It is, therefore, important to note that the reflex fall in heart rate and blood pressure produced by other substances cannot be regarded as manifestations of the Bezold-Jarisch effect – a mistake that is often made in various accounts published in text books of physiology or published papers. The receptors involved in this reflex are firstly the ventricular pressure receptors with medullated fibres which were discovered in 1955 (Paintal 1955b). The justification for this conclusion was that these receptors were stimulated by veratridine and veriloid with different latencies, respectively. These latencies corresponded to the latencies for the occurrence of reflex bradycardia and, therefore, it was concluded that these receptors were responsible for the Bezold-Jarisch effect. Subsequently, Coleridge *et al.* (1964) and Sleight & Widdicombe (1965) found that the epicardial receptors with non-medullated fibres were also stimulated by veratridine and they concluded that these C-fibre receptors were responsible for the Bezold-Jarisch effect. The controversial issue was again taken up by Paintal (1973a) in his report wherein he showed that the receptors with non-medullated fibres could not be responsible for the Bezold-Jarisch effect on the basis of the reflex effects produced by nicotine, phenyl diguanide and veratridine. In support of the fact that in the cat the Bezold-Jarisch effect is caused by ventricular pressure receptors with medullated fibres, is the observation of Dawes, Mott & Widdicombe (1951) that the reflex is abolished by cooling the Vagi to 11-8°C. Since the reflex effects produced by receptors with non-medullated fibres is blocked at much lower temperatures of about 2-4°C (Paintal 1967) it follows that the Bezold-Jarisch effect in the cat is produced by ventricular receptors with medullated fibres.

Cardiovascular receptors

There has been some interest in India in the field of sensory receptors located in the heart and major vessels, mostly in atrial receptors. This began with the re-investigation of the natural stimulus of the atrial type B receptors after the publication of two papers by Langrehr (1960a,b) in which he concluded that the stimulus for the type B receptors was ventricular contractions. Through systematic experiments, Paintal demonstrated that the natural stimulus for the type B receptors was the filling of the

atrium as manifested in the V wave of the atrial pressure curve (Paintal 1963). By using timed ventricular extra systoles he showed that the effect of the extra systoles on the type B receptors differed depending on whether the receptors were located in the right or left atrium. They differed to such an extent that, as shown by Fahim (1977), it was possible to identify the probable location of type B atrial receptors without opening the chest in the right or left artium by using ectopic stimulation of the right atrium through a stimulating electrode inserted through the external jugular vein of dogs. In a related paper, using controlled time injections of fluids into the atrium, Fahim showed that the amplitude of the V wave was related to the volume of fluid injected. This linear relation of the amplitude to the volume injected also extended to low volumes of injection (Fahim 1978). Finally, he (Fahim 1979) showed that the relationship between the V wave pressure and the activity of type B atrial receptors was qualitatively unchanged with lowering the temperature by about 10°C. However, although the linearity remained unchanged there was a fall in activity of the receptors, the Q_{10} being about 2.5. This was similar to Q_{10} reported by Paintal in the case of the pulmonary stretch receptors and aortic chemoreceptors (Paintal 1971).

With a view to determining the nature of the effective stimulus for the type A receptors, Rao & Fahim (1976) studied the effect of reducing the contractility of the myocardium by injections of large doses of propranolol on the activity of the type A receptors. They found that at least part of the depression of the activity by propranolol is due to the direct depression of the receptors itself.

Differences between type A and type B receptors

The Leeds group of workers have, in spite of evidence to the contrary, maintained that there is no difference between type A and type B receptors and that the two constitute essentially one type of receptor (See Linden & Kappagoda 1982). However, others have not accepted this view and proceeded to find out the reasons for the difference in the drastically different patterns of discharge in the type A and type B receptors. B.N. Gupta showed clearly that there was no difference in the locations of the two types in the right and left atrium (Gupta 1977a) or in the adaptation rates (Gupta 1977b, 1978). The mechanism underlying the difference remains unknown.

Coronary artery mechanoreceptors and pulmonary artery baroreceptors

Paintal (1972) has argued convincingly that the possible existence of mechanoreceptors in the coronary arteries (Brown 1965) and pulmonary artery baroreceptors (Coleridge & Kidd 1961) is small as the receptors concerned do not bear a close relationship to their presumed natural stimulus, namely the pressure pulse in the coronary arteries and pulmonary artery, respectively. He pointed out that the conclusion of Coleridge & Kidd (1961) regarding the existence of pulmonary artery baroreceptors arose probably because the investigators did not attach primary importance to the relation of the natural stimulus (i.e. pressure pulse) to the pattern and intensity of discharge but instead they attached over-riding importance to the results obtained

by punctate location of the receptors.

Afferent fibres in sympathetic nerves

Koley *et al.* (1985) recorded impulses from afferent fibres running in the sympathetic nerves (sympathetic rami-T_2-T_4) of cats. These originated from high threshold baroreceptors located in the brachiocephalic artery and the descending aorta. Two distinct types of receptors, type I and type II, were found. The results were in general similar to those obtained earlier by others. Later, Koley repeated the experiments in monkeys and obtained results similar to those they obtained in cats (Koley *et al.* 1989).

Using the same techniques for recording from sympathetic fibres, Pal *et al.* (1989) recorded impulses with fibres running in sympathetic nerves arising from receptors located in the coronary arteries. About a third of these receptors were stimulated by occluding the coronary arteries. These receptors were also stimulated by so-called algesic agents, namely lactic acid, bradykinin, prostaglandins, and nicotine. According to the authors these receptors were probably responsible for the pain of cardiac ischaemia.

RESPIRATORY PHYSIOLOGY

Methodology: New developments in the field of respiratory dynamics

Two important contributions have been made for determining specific airways conductance (sGAw). One is that Agrawal & Kumar (1980) have provided a method for determining sGAw during normal breathing without having to make the subject breathe rapidly. This method is therefore applicable to animals also since they cannot be made to pant. Using this method it has been shown that the determination of sGAw at residual volume is probably the most sensitive method for the early detection of small airway obstruction in man.

Agrawal (1981) has also developed an ingeneous box method for measuring sGAw in guinea pigs. This box is commercially available internationally. At present this method (i.e. Agrawal's box) is the most commonly used method for measuring sGAw in intact conscious guinea pigs.

High Altitude Physiology

The need for research in high altitude physiology became apparent at the time of the Indo-Chinese conflict in 1962. There arose an urgent need to understand the mechanisms underlying acclimatization to high altitudes, the various disorders that developed when people were taken up to high altitude quickly by air, the mechanisms underlying high altitude pulmonary oedema (HAPO), how it could be prevented and how it could be cured once it developed. A number of studies supported by the Indian Council of Medical Research and the Director-General Armed Forces Medical Services, were launched. Notable amongst these were the studies by Singh (1965, 1967, 1969)

and those led by Roy (1968, 1969). A study by Menon (1965) and one by Lal (1967) provided valuable data. Menon concluded that HAPO was due to left ventricular failure. This view was not supported by Roy who found that the wedge pressures were not raised although the pulmonary artery pressures were raised considerably (Roy *et al.* 1969). This point was reviewed by Menon (1984) who felt that the possible occurrence of left ventricular dysfunction would not be brushed aside.

Certain investigations in laboratories at sea level were also carried out. For example, with a view to elucidating the cause of HAPO, Vishwanathan and his co-workers studied certain physiological responses of normal subjects and those who had developed HAPO with special reference to the occurrence of rise in pulmonary artery pressure during hypoxia (Vishwanathan *et al.* 1969b). They also studied the responses of animals during simulated altitude (Vishwanathan *et al.* 1969a). From all these observations, Vishwanathan *et al.* (1969c) developed a theory based on precapillary constriction of pulmonary arterioles during hypoxia to explain the occurrence of rise in pulmonary artery pressure during hypoxia. In a later study, Vishwanathan *et al.* (1976) applied the same hypothesis to the rise in pulmonary artery pressure produced during hypercapnia.

Pulmonary receptors and their reflex effects

Pulmonary Stretch Receptors. Contrary to earlier beliefs it was shown that the majority of slowly adapting pulmonary stretch receptors were located in the lung parenchyma (Paintal & Ravi 1980, Ravi 1986) and that they were mostly accessible through the pulmonary circulation. Ravi (1986) suggested that there were noteworthy differences between the low threshold and high threshold receptors. He also showed that both the slowly and rapidly adapting receptors were depressed by CO_2 as had been reported in the case of the receptors of the dogs. The opposite, i.e. lowering the arterial CO_2 tensions stimulated the receptors (Ravi 1985). Earlier, Fahim & Jain (1979) had observed that the low threshold PSR's were blocked earlier than the high threshold SARS & RARS by Bipivacaine aerosol. In this connection it is worth noting that earlier, Paintal (1966) had shown that it is because of the activity in the lower-threshold pulmonary stretch receptors that Head's Paradoxical reflex appears on cooling the vagus to 12-8°C. At this temperature inflation blocks the discharge in the lower-threshold receptors thus causing stimulation of inspiration, i.e. paradoxical stimulation of inspiration on inflation of the lungs.

J Receptor Physiology

The first J Receptor was discovered on 24 May, 1954 (A.S. Paintal, personal communication). Initially they were called pulmonary deflation receptors (Paintal 1955a) and their rough location was established soon afterwards (Paintal 1957). The next significant publication on this subject appeared in 1969 when Paintal (1969) showed that the receptors were actually located close to the pulmonary capillaries at the alveolar level and he therefore called them Juxta-pulmonary capillary receptors, i.e.

type J receptors and showed that these receptors were stimulated during pulmonary congestion and pulmonary oedema and that they were therefore involved in producing breathlessness as proposed following his earlier observations (Paintal 1955a). He also showed that they produced reflex inhibition of somatic muscles. This reflex he called the J reflex (Paintal 1970). Deshpande & Devanandan (1970) showed that this reflex affected all the muscles they tested through the monosynaptic reflex and that it was abolished after decerebration, thereby indicating that pathways rostral to the midbrain were involved in the J reflex. Kalia tried to localize the region of the cerebrum concerned with the reflex. She found that the caudate nucleus and the cingulate gyrus seemed to be essential for the reflex to operate (Kalia 1973, 1974). This subject was reviewed by Paintal (1973b).

The fact that the discharge in J receptors often consisted of intermittent bursts of impulses (Paintal 1969) and that histamine affected this activity led Paintal (1974) to suggest that there is a fluid pump involved in the generation of the intermittent bursts. He showed that the excitation by histamine of the J receptors followed a different time course (Paintal 1977). This was discussed subsequently by Paintal & Anand (1984). They showed that histamine lowered the threshold of the J (and other) receptors and thus revealed subthreshold activity in them. They also showed that histamine enhanced the excitation produced by phenyl diguanide (Anand & Paintal 1980). The stimulation of J receptors by histamine was used by Singh *et al.* (1982) to show that the histamine induced bronchoconstriction could be partly attributed to activity in J receptors.

In a related work Paintal, Damodaran & Guz (1973) showed that the J receptors were stimulated mechanically during pulmonary embolism.

An important advance in J receptor physiology took place in 1980 when Anand & Paintal (1980) published their paper describing the phenyl diguanide dose-response relation of the J receptors and showed that the J receptors were stimulated by increase in pulmonary blood flow; increase in cardiac output by about two times produced on the average 0.7 impulses/s. This was a significant discharge as this intensity of discharge produced marked respiratory and somatic reflex effects which could be conclusively attributed to the J receptors after ensuring that cardiac receptors were blocked by injecting xylocaine intra-pericardially so as to block all the cardiac nerve fibres involved.

Ravi (1988) also studied the reflex effect of J receptors after injecting xylocaine into the pericardial sac of dogs. He used capsaicine and concluded that apart from the heart and lungs, there was a reflexogenic zone in the splanchnic bed that produced apnoea in vogotomized dogs on injection of capsaicine into the adbominal aorta in dogs with spinal transection at L4-L5 level. Before spinal transection, the effect produced was hyperpnoea. A useful observation made by Ravi & Dev (1988) was that metoclopramide blocked the reflex effects produced by pdg and 5HT but did not block the effects of capsaicine.

A major contribution was made by Jain *et al.* (1972) when they demonstrated that

the reflex respiratory effects produced by lobeline in man were due to stimulation of the J receptors.

Substantial evidence obtained from observations on human volunteers using lobeline and observations on soliders who suffered high altitude pulmonary oedema led to the suggestion that the J receptors produced certain sensations of irritation in the throat and that this led to dry cough when the sensations became more intense; pain in chest was also produced in several subjects (Paintal 1986). Jain (1980) had observed that cough is seen in laryngectomized subjects after injections of lobeline. The fact that the J receptors produced inhibition of somatic muscles and that they also produced breathlessness, led Paintal to show that breathlessness, dry cough and muscle weakness constituted an important triad of effects of J receptor stimulation and one that was clearly manifested in the victims of the Bhopal gas tragedy (Paintal 1986).

The most recent advances in J receptor physiology have come about following the discovery of the principle of the relative dilution of multiple solutes in flowing fluids (Paintal & Anand 1991, 1992). As a result of this discovery a method for recording *in vivo* the concentration of injected substances was evolved. Thus, since it was now possible to measure in pulmonary capillary blood, the concentration of injected excitants of J receptors it became possible to show that such excitants (and injected solutes in general) move out of the pulmonary capillaries through forces of diffusion, not filtration (Paintal & Anand 1992). An equally important advance made as a result of the new technique for measuring *in vivo* the concentration of excitants, was that the permeability increase that occurs during pulmonary oedema leads to a greater movement of the excitants across the capillaries to the J receptors leading to their greater excitation (Anand, Paintal & Whitteridge 1993). It is likely that this increase in the stimulation of the J receptors will be directly related to the increase in permeability thus making it possible to obtain an assessment of increase in permeability under various pathological conditions in man – a possibility that had been suggested earlier (Anand *et al.* 1989).

Arterial Chemoreceptors

It would not be an overstatement to say that the greatest amount of significant work on aortic chemoreceptors has been carried out in India. Beginning with the demonstration by Paintal & Riley (1966) that there were no chemoreceptors in the pulmonary artery, they went on to show that CO_2 did not stimulate the aortic chemoreceptors. This fact was proved more elegantly with measurement of arterial CO_2 tensions in the arterial blood later by Anand & Paintal (1988). They pointed out that the stimulation seen earlier by other investigators was probably due to a greater amount of sympathetic activity in their cats owing to use of neuro-muscular blockers. The role of the sympathetic had been earlier shown by Anand (1979) by her observations on the effect of stimulating the receptors in the intestines on the stimulation of the aortic chemoreceptors, an effect that was greatly reduced or abolished by removing the stellate ganglion and the adrenal glands.

Mechanisms of Stimulation of Chemoreceptors

A major advance made regarding the mechamisms of stimulation of chemoreceptors was the demonstration that the metabolic theory (i.e. stimulation by liberated metabolites) was not valid (Paintal 1967a). He also showed that acetylcholine could not be a transmitter at chemoreceptors since it did not stimulate many aortic chemoreceptors with medullated fibres (A fibres) and that it stimulated the ones with non-medullated fibres (C-fibres) far more effectively. He, therefore, proposed that the aortic chemoreceptors were stimulated through some sort of deformation of the type II cell – the sustentacular cell. This is known as the mechanical hypothesis. Later Fidone & Sato (1969), using an unusual method for recording impulses (the monotopic technique), contested Paintal's results by showing that carotid chemoreceptors with A fibres were far more sensitive than the carotid chemoreceptors with C fibres (Fidone & Sato 1969) i.e. the opposite of what Paintal had reported (Paintal 1967b). However, later through further experiments using their monotopic technique, Paintal (1988) showed that the monotopic technique used by Fidone & Sato yielded artifactual results. Moreover the data obtained by them could not be reconciled with the data on the histological composition of the carotid nerve obtained by Eyzaguirre & Uchizono (1961) and earlier by De Castro (1951). Paintal has pointed out that considering these results, showing that the chemoreceptors with non-medullated fibres, are far more sensitive to excitants than chemoreceptors with medullated fibres implies that for any chemical to be regarded as a transmitter it must stimulate receptors with both types of fibres equally. However, the majority of chemoreceptorologists believe that there is a transmitter at chemoreceptors and it is therefore clear that more evidence in favour of the mechanical hypothesis will be needed before chemoreceptorologists change their views on the mechanism of stimulation of arterial chemoreceptors.

Role of hypotension

It is generally believed that hypotension is not an important stimulus for chemoreceptors. This is because most investigators have worked on carotid chemoreceptors and because of certain observations by Biscoe, Bradley & Purves (1970). However, in the case of aortic chemoreceptors it has been shown clearly that hypotension is a very effective stimulus for them (Anand & Paintal 1988). Using these observations Anand & Paintal (1990, 1991) have formulated a mechanism by which hypotension stimulates chemoreceptors.

Effect of muscle receptors on respiration

A significant contribution from India was the finding by Senapati (1966) that stimulation of pressure pain receptors of muscles (Paintal 1960) with a pressure applicator to the gastrocnemius muscle of dogs resulted in stimulation of ventilation. This constituted the possible mechanism of the early hyperpnoea of exercise. Subsequently he and his collaborators showed that the carotid chemoreceptors played no role in this stimulatory effect. Still later he showed that this effect was much reduced after cooling

or ablating the anterior lobe of the cerebellum (Panda *et al.* 1979). Similar reduction of respiratory stimulation was seen on the excitatory influence of CO_2 on respiration by ablation of the anterior lobe of the cerebellum (Senapati *et al.* 1990). In related experiments Kalia *et al.* (1972) showed that stimulation of non-medullated muscle afferent fibres produced stimulation of respiration.

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PHYSIOLOGY OF REPRODUCTION

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The last few decades have witnessed far reaching changes in human reproductive behaviour. Population is doubling now in a record time of only 30 years in some parts of the world including India. Being seized of the gravity of the situation, innovation of more reliable, acceptable and safe contraceptives has become an attractive area of biomedical research for a country like India which faces the serious challenge of a high birth rate neutralising all developmental efforts.

CONTRACEPTION : PHYSIOLOGICAL PRINCIPLES AND DEVELOPMENT OF NEW APPROACHES

One of the most significant contributions from India in this field is the centchroman based once-a-week oral contraceptive pill for women, introduced in 1991 under the trade name of 'Saheli'. It is the world's first non-hormonal contraceptive pill and is the result of more than 20 years of research by VP Kamboj, AB Kar and their colleagues (1971). Centchroman inhibits implanation by its antiestrogen action in doses of 30 mg every week and the antifertility effect is readily reversible. Several countries, particularly South Korea, are showing interest in manufacturing this new contraceptive.

Considerable progress has also been made in the newly emerging field of immunology of reproduction and pregnancy vaccines. The group led by GP Talwar (1976, 1980, 1992), firstly at AIIMS and later at Indian Institute of Immunology (III), New Delhi has evolved a vaccine against the B-subunit of hCG molecule. The B-subunit is unique to this placental hormone, while its A-subunit is common with the pituitary FSH, LH and ACTH. The antigenicity of B-hCG has been enhanced by combining it with tetanus toxoid or other similar bacterial proteins. Three primary immunisations every 6 weeks and a booster dose as required later can maintain a level of antibodies in the blood which would effectively neutralise any hCG coming from the fertilised ovum. In the absence of this physiological signal to the ovary, there is no attempt to prevent the next menstrual bleeding and pregnancy cannot continue. Extensive work on this pregnancy vaccine has also brought out some of its limitations (Talwar *et al.* 1989). Recent trials have shown that not all immunised women respond with acceptable titres needed to block fertility, possibly because of some genetic differences.

Immunisation against GnRH is also being tried by GP Talwar as this 'master molecule' controls the cascade of events regulating reproduction and steroidogenesis

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(Talwar & Sad 1990). Physiologically, it has two advantages. Firstly, it would be effective in both men and women. Secondly, this decapeptide molecule has passed virtually unchanged through its long evolutionary history and, therefore, antibodies against it would be effective in a wide range of mammalian species.

Moudgal and his colleagues at IIS, Bangalore have been focussing their attention on FSH and the possibility of contraceptive vaccines based on this (Sivashankar *et al.* 1977). However, Nieshchlag (1986) has pointed out that immunisation against FSH is unlikely to succeed since FSH is needed for initiation of spermatogenesis but perhaps not for its maintenance.

An unconventional route of administration for minimising the amount of sex steroids needed to inhibit ovulation has been tried by TC Anand Kumar (Anand Kumar *et al.* 1980, Moudgal *et al.* 1985). Intra-nasal micro quantities of single steroids, combinations and in different dose regimes have been tried in rhesus monkeys at AIIMS and a 50% success rate in blocking ovulation has been reported. Obviously, there could be problems of an uncertain and individual variable absorption from the nose besides the possibility of damage to the mucosa on a long-term use.

Male reproduction has in-built limitation as far as contraception is concerned. There is always the risk of interference with male libido and mating behaviour – a fundamental prerequisite for mammalian reproduction. Therefore, the safest sites appear to be the vas and beyond, where sperm transport can be mechanically blocked by vasectomy or condoms.

Although vasectomy now constitutes only about 6% of all sterilisation operations in India, it still remains the most dependable contraceptive for males in a global perspective. A disconcerting recent finding from the UK is that there may be a relationship between vasectomy and testicular tumours (McDonald 1990). Also, factors like species differences, age of the animals, vascular injury during surgery, infection, observational errors etc. markedly influence the magnitude of post-vasectomy changes other than sterility. LK Kothari and his colleagues found a significant depression of spermatogenesis 4 weeks after vasectomy (Gupta *et al.* 1975); but repeat biopsies taken 2 to 3 years later showed that spermatogenesis was again within normal limits and the testes had adjusted itself to the vasal block. However, it is ultimately the blood testosterone level which matters. Naik *et al.* (1976) found no significant change in hormone levels after vasectomy in human subjects. PK Devi, AR Sheth and their colleagues at IRR, Bombay have also monitored the hormone profile of 180 vasectomised men (Devi *et al.* 1977). No change was found in plasma LH, FSH and estrogen, but testosterone showed an interesting post-vasectomy rise in the age group of 41-45 years.

Finally we can turn to our vast heritage of folklore and traditional medicine which contains many references to contraceptive herbal formulations. This has inspired exploratory screening of a large number of indigenous plants for a safe contraceptive. The outcome of their pharmacological screening has been reviewed by VP Kamboj

(1988). GP Talwar (1990) has recently reported a prolonged anti-implantation effect of neem oil with a single intra-uterine application. This is a novel approach and needs further follow up.

Several other contraceptive methods being tested in India are of physiological interest although their ultimate usefulness is difficult to predict. For example : non-occlusive copper wire in the vas (Laumas *et al.* 1979) and progesterone scrotal implants (Srivastava 1981).

ANDROLOGY : BASIC AND CLINICAL

The study of maleness and its problems – ANDROLOGY – has yet to find recognition as a speciality in its own right in India despite some good work, both at the basic and clinical levels, done during the last 2 decades.

Hormonal Regulation

Inhibin : One arm of the feedback system which connects the pituitary and testes has remained elusive for long: the signal from the seminiferous tubules which limits FSH release.

Sheth *et al.* (1978, 1979) developed one of the earliest bioassay techniques for inhibin based on suppression of hCG-induced increase in the weight of reproductive organs of mice, and later a sensitive RIA system for human inhibin. The question whether inhibin has any other physiological functions besides inhibiting FSH release has also been examined. The amount of inhibin riding on the sperms as a surface coating has shown positive correlation with sperm motility on flow cytometric analysis (Bandivdekar *et al.* 1989). Poor sperm motility is sometimes the prime defect in male infertility and it would be pertinent to study the role of inhibin in such patients. Sheth *et al.* (1981) reported a sharp rise in inhibin 2-4 days before the LH peak in normally menstruating women. It appears that inhibin has a role in the feedback suppression of FSH in the female also.

The role of hypothalamic GnRH in stimulating pituitary-gonadal function is well established but Ravindranath and Moudgal (1987) have shown that continuous infusion of GnRH agonists desensitises the pituitary to GnRH. Thus, male monkeys become almost azoospermic. Theoretically, male contraception seems possible by implants which continuously deliver micro quantities of a GnRH agonist plus some testosterone to maintain libido.

Prolactin: The physiological role of prolactin in the male remains a matter of curiosity. Sheth *et al.* (1975) estimated prolactin in the human seminal plasma and, surprisingly, found levels 4 to 7 times higher than in the blood. The seminal vesicles and prostate seem to concentrate prolactin in their secretion. The role of prolactin in stimulating testosterone secretion and sperm motility is also gradually emerging. These

actions may correspond to an evolutionary LH-like luteotrophic role of prolactin in lower mammals.

Prolactin is also shown to have a direct stimulatory effect on the epididymis and other accessory sex glands, apart from its indirect action through testosterone release. Reddy *et al.* (1985) have found that bromocriptine, which markedly lowers blood prolactin, leads to depression of epididymal metabolism even though the blood testosterone level is unchanged. On the other hand, Tripathi & Mukhopadhyaya (1987) have shown that pituitary homografts placed under the renal capsule of castrated young rats can prevent accessory sex gland atrophy. It is reasonable to presume that this is because of prolactin coming from the graft.

Leyding Cells: A method for computing the size of the endocrine testes, or Total Leyding Cell Volume (TLCV), applicable to human subjects has also been developed by LK Kothari and his co-workers for quantitative studies under a variety of conditions (Kothari *et al.* 1972, 1978). It was interesting to find a significant increase in the TLCV in elderly men (Kothari & Gupta 1974). This was contrary to the commonly held view that there is an age-related involution of the Leyding cells which is responsible for the declining androgenic and anabolic drive in elderly men.

EPIDIDYMIS

MRN Prasad and his colleagues have carried out extensive studies on the physiology of the epididymis in laboratory animals at the Department of Zoology, Delhi University (Rajalakshmi *et al.* 1976). An interesting fact has emerged that the epididymis requires higher androgen concentration for its structural and functional integrity than other accessory glands. These observations have led MRN Prasad to try a synthetic antiandrogen, cyproterone acetate, as an oral contraceptive for men (Prasad *et al.* 1970), which interferes with epididymal capacitation of sperms.

LK Kothari has also studied the cyto-architectural differences within different parts of the epididymis and correlated them with function (Patni & Kothari 1984). The size of the epididymis in relation to the testes, or the ratio between the volume of testicular secretion and the epididymal absorptive capacity, has been suggested as an important determinant of the extent of testicular changes that follow vasectomy in a particular species.

SEMINAL BIOCHEMISTRY

Extensive work on a recently discovered antimicrobial protein in the seminal plasma, seminalplasmin, has been carried out under PM Bhargava at the CCMB, Hyderabad (Chitnis *et al.* 1987). It can lyse a wide range of bacteria and yeasts besides the sperms themselves. Its action appears to be normally held in check by antiplasmins. Can a change in seminalplasmin level explain some types of male infertility is an interesting question which needs further study. Seminalplasmin could also be a starting

point for a type of contraceptive – a physiological sperm destroying agent.

FEMALE REPRODUCTION

Brain & Reproductive Behaviour : S Dua-Sharma & KN Sharma (1973) created stereotaxic lesions in several forebrain structures of monkeys and found that this disturbs the gonadotrophic secretion and, consequently, the ovarian cycle. Both facilitatory and inhibitory neural substrates exist. This indicates a dual control of the estrus cycle – hormonal and nervous. It could also explain, at least in principle, how a variety of emotional stresses can upset menstrual cycle in women. Working on feedback control of genital receptors it was clearly shown that genital afferents not only project to discrete central nervous regions (CNS) implicated in reproductive behaviour, but also influence their activity. There is a two-way interaction been peripheral inputs and CNS and modulated by environmental features and neuro-humoral milieu at multilevels (Dua-Sharma *et al.* 1977).

Interesting observations in relation to the Hypothalamic-Releasing Hormones which regulate FSH and LH release have been made by OP Tandon & SK Manchanda (1976). It seems that LH-RH leaking into the CSF from the adjacent arcuate nucleus may act as a modulator of this response. Infusion of LH-RH directly into the third ventricle of rats markedly increased the arcuate nucleus activity. This could be a good example of a hormone acting through a short-loop positive feedback for building up its own release into a powerful surge. It is well known that such a LH surge is essential for ovulation.

If the brain influences reproductive behaviour, the converse is also true in good measure : sex hormones influence brain mechanisms. Borkar & Gogate (1984) have studied the effect of sex steroids on hoarding behaviour of female rats. Several species are known to hoard food and this is most marked in proestrus. Estrogen microinjections into the preoptic area increased the hoarding tendency while progesterone decreased it. Similarly, KN Sharma has brought out a relationship between the taste preference of female rats and the phase of their estrus cycle. On the day of the estrus, they exhibit a clear preference for sweet solutions (Kanaka *et al.* 1979). A similar modulation of taste has been observed in human females during menstrual cycle (Bhatia *et al.* 1981). If sex hormones affect central gustatory processes, it can help us understand why pregnant women show peculiar changes in their food preferences. In India, this is sometimes taken as a sign to diagnose pregnancy and even to predict the sex of the baby – a point which may be worth exploring further.

Equally interesting is the relationship between pain perception and sex hormones (Rao *et al.* 1987). Estrogen and progesterone desensitise the pain apparatus while a relative fall in their level, as during menstruation or after ovariectomy, gives a heightened pain sensitivity. Perhaps it is an evolutionary adaptation which makes the female more tolerant to the pain associated with their reproductive responsibilities.

Hormonal Regulation: Progesterone is well established as the hormone of

pregnancy but now the supportive role of estrogen is also gaining importance. SK Manchanda & colleagues (1984) have shown that estradiol-17B is essential for early implantation and embryonic differentiation. Ravindranath & Moudgal (1987) have confirmed the role of estrogen in early pregnancy in monkeys by giving them the antiestrogen, tamoxifen, which resulted in abortion.

What triggers the onset of puberty at the appropriate age is something that is not yet fully understood. The presence of a gonadotropin-inhibiting factor (GIM) in the urine of young boys and girls has been suspected since 1960. Work at the Cancer Research Institute, Bombay has shown that GIM possibly originates in the hypothalamus and acts by blocking gonadotropin binding at the target cells. It fits into the generally held view that puberty is triggered by a release of the hypothalamus – pituitary – gonadal axis from one or several inhibitory influences which gradually weaken as childhood progresses.

Immunology: The immunological aspects of fertility have been engaging the attention of several centres in India. Prominent among these are the IRR Bombay, AIIMS New Delhi, IIS Bangalore and the more recently established NII New Delhi. The main emphasis is on innovation of new contraceptive approaches and an impressive contribution is being made in this field in a global perspective. hCG produced by the placenta, non-hormonal trophoblastic antigens, zona pellucida proteins, pituitary gonadotropins and sperm antigens are all being worked upon from this angle (Talwar 1980).

Fallopian Tube Function: SK Manchanda & colleagues (1979) at AIIMS, New Delhi have elaborately studied the motility of the oviduct in conscious rabbits after permanently implanting a plethysmographic device round the tube. Ovulation induced by hCG injection led to a three-phase change: a) receptive relaxation for 8-12 h; b) increased isthmic motility reaching a peak at 48 h; and c) restitution of original state. It seems that the Fallopian tube has an important role to play in the proper timing of the two critical events of fertilisation and implantation. Too slow or too rapid transit of the ovum can both lead to ultimate reproductive failure. That the regulating signals to the Fallopian tube are hormonal and not nervous can be deduced from the studies of Rajkumar & Sharma (1978) in rats. Autonomic drugs do not have any appreciable influence on normal conception and delivery.

REPRODUCTIVE PHYSIOLOGY IN CLINICAL MEDICINE

Benign hypertrophy of the prostate (BPH) is so common in the elderly that it can be considered almost a normal component of ageing in the male. Narayan *et al.* (1985) have isolated 14 steroid fractions from prostatic homogenates. They found that some estrogen and progesterone fractions were present only in BPH. It is likely that steroids produced by the testes are converted to estrone and estriol by the prostate and these are responsible for the hypertrophy. Interestingly, inhibin has also been found in large quantities in BPH and it inhibits the conversion of testosterone to dihydrotestosterone

(Sheth *et al.* 1987). These studies have practical relevance because there is a need for some drug as an alternative to prostate surgery and, if possible, for the prevention of BPH altogether.

The chance observation by LK Kothari and his colleagues that the widely used antibacterial drug, cotrimoxazole, can lead to suppression of spermatogenesis in human subjects has drawn attention to the general problem of drug-induced infertility in the male (Murdia *et al.* 1978). Cotrimoxazole is a combination of a sulphonamide and trimethoprim and sequentially interferes with folic acid metabolism. Another sulphonamide, sulfasalazine or salzopyrin, is being seriously considered as a possible male contraceptive.

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ERGONOMICS AND WORK PHYSIOLOGY

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The word 'ergonomics', first coined by the members of the Human Research Society in early 1950s, aims to study man's behaviour in relation to his work, and encompasses the science, technology and art of man at work. With the realisation of 'human use of human resources', interfacing of engineering and materials technology with human technology has opened up newer vistas. Ergonomics is recognised today as an interdisciplinary science; it bases its theories on physiology, psychology, anthropometry, various aspects of engineering and biomechanics.

The problem of ergonomics are not new; but all the problems have emphasised that the technical developments have reached the state at which the capacities of the operator rather than the potentialities of his equipment are setting limits to the performance of men and machines working together. It is therefore necessary that these human limits should be studied and machines should be designed in relation to them.

Since the early development of the subject, its application has widened to include several areas. Currently ergonomists emphasize both on products of all kinds — domestic, commercial or military, and on the processes that generate these products. Further it has been felt that under the conditions of the scientific and technological revolution, an increasingly important social and economic value has to be attached to ergonomics because of its implications for man and society.

Growth of Ergonomics Research in India

The Physiology Department of the Presidency College, Calcutta, was the first to start work in Industrial Ergonomics in India in 1953, at a cotton textile mill in West Bengal (Sen 1984). In the year 1962, almost simultaneously, the Industrial Physiology Divison in the Central Labour Institute, Bombay and the Defence Institute of Physiology and Allied Sciences, Delhi, started work in the field of work physiology and ergonomics, pertaining to various categories of factory workers and armed forces personnel, respectively.

Presently, in addition to the premier institutes mentioned above, researches in the different areas of ergonomics are being conducted in the Ergonomics Laboratory of the Physiology Department of the University College of Sciences & Technology, Calcutta; Ergonomics and Occupational Health Division of the All India Institute of Hygiene and Public Health, Calcutta, Ergonomics Laboratory of the National Institute of Occupational

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Health, Ahmedabad; Industrial Design Centre, IIT, Bombay; National Institute of Training for Industrial Engineering, Bombay; National Institute of Design, Ahmedabad, and Physiology Division of the Netaji Subhash National Institute of Sports, Patiala and its regional centres under Sports Authority of India. Recently, several industries have also started their own ergonomics and occupational health units, which mostly look after their own problems. These units are National Model Centre for Occupational Health Services, BHEL, Tiruchirapalli, the Occupational Health Units in different steel plants under Steel Authority of India; the Railway Design and Standards Organisation RDSO, Ministry of Railways, Lucknow; and very recently the different refineries of Indian Oil Corporation, India.

Energy Expenditure Studies

The study of energy expenditure in some sedentary and industrial workers of different categories was initially undertaken by Banerjee *et al.* (1959) to know about the physical strain, optimum work load and calorie intake in these subjects while performing the work. BMR values of the Indians were found to be much lower than Mayo Foundation readings.

The energy costs of different activities of a cotton textile mill (mixing, sizing and weaving departments) and of a soap factory in Bombay were found to vary from 1542 to 3647 kcal and 2173 to 3679 kcal respectively (Sen *et al.* 1964a, 1964b). Allowing natural ventilation improved work load and transformed uncomfortable conditions to comfortable ones (Majumdar 1985).

Similarly, the energy cost of different activities in a steel rolling mill, the energy costs of handling heavy loads of unorganised porters (Sen & Nag 1974, 1975) and a group performing agricultural work and another group undertaking fast printing work were also studied (Nag *et al.* 1978). These energy expenditure studies gave an idea about the work load and nutritional requirements of different types of tasks in agricultural, industrial and general environments.

A number of studies on the nutrition and calorie requirements of the various categories of personnel in Indian Armed Forces which constitutes the largest employment sector in our country have also been conducted. The daily energy expenditure of the Infantry and Artillery personnel at altitudes in the Eastern and Western sectors, ranging from 3600 to 3960 m, was found to be between 3371 kcal and 3408 kcal. Similar energy expenditure studies were carried out on troops, at higher altitudes (4000 m and 4600 m) for peace and field areas (Malhotra *et al.* 1970), for submarine crews both in sailing and exercise group (Malhotra *et al.* 1972), for ambulatory and non-ambulatory groups of patients (Nayar *et al.* 1979), for boys in the age groups of 11-16 yrs in the Sainik and Military Schools (Sridharan *et al.* 1979a), for various tradesmen and pioneers in Borders Road Organisation (Sridharan *et al.* 1979b) and very recently for the coast guard (Sridharan *et al.* 1992). These studies helped in the formulation of proper nutritional scale of the Armed Forces personnel engaged in various tasks and

in different climatic conditions, to keep them fighting fit. The energy expenditure of snow clearance around the living station in Antarctica was also studied (Majumdar 1992).

Optimization of Loads

Interest in the military, industrial and general aspects of individual load carriage is long-standing. As early as 1964 Ramaswamy *et al.* studied oxygen consumption in load march as influenced by the magnitude of the load carried as well as the steepness of the terrain crossed. The physiological optimum speeds at which the energy cost of carrying out a given amount of work was found to be about 4.8-5.6 km h^{-1}. Based on the findings, optimum value of carrying load for steepness of gradience, nature of terrains and speed of march has been predicted.

Datta & Ramanathan (1970) studied the subjects who climbed stairs at a fixed rate with external loads ranging from 0 to 30 kg on the head, and concluded that an upper limit of 30 kg should be recommended for load carrying upstairs by a single average Indian. The same authors (Datta & Ramanathan 1971) studied the physiological responses of seven modes of carrying an identical load on the level ground and found the double pack mode to be ergonomically the best mode, followed closely by the head mode. Sen & Nag (1975) ascertained the physical work rate, the energy and cardiac costs of 27 young male workers in five groups handling five different work loads with the objective of rationalizing the rate of work. The workers were found to be working at levels much higher than 50% of their maximal physical work capacity. Twelve hundred kcal was suggested as the net optimal energy output in an 8 h working day, for extremely heavy types of work in India.

In an attempt to find out the optimal rate of work for mountaineers, Nag *et al.* (1978) suggested that for day-to-day operation the highlanders and porters should not work more than 30 to 40% of maximal work capacity, a rate of work around 4000 kg m min^{-1} (25-30 kg actual load at 3.0 to 3.5 km h^{-1}). Saha *et al.* (1979) proposed that an acceptable work load for average young Indian workers in comfortable thermal conditions should not be more than 35% VO_2 max. corresponding to 18.0 Kj min^{-1} energy expenditure (or 0.881 min^{-1} VO_2) and 110 beats min^{-1} for heart rate.

The effect of age variation on load-carrying ability was studied by Samanta *et al.* (1987). They found that the maximum permissible load carried on the head by groups of Indian porters ranging in age from 20 to over 50 yrs, decreased from 41 kg for the youngest group to 11 kg for the oldest.

Unorganized workers, including those in agriculture, have many problems which could be solved using ergonomic principles but unfortunately very little is done. Nag *et al.* (1980) attempted to evaluate the workload and categorization of the Indian agricultural workers based on cardiorespiratory parameters. The study of Sen *et al.* (1981, 1983) on tea leaf plucking indicated that the application of ergonomic principles

resulted in (i) a reduction in workload and improvements of work methods, (ii) a recommendation for the selection of bush dimensions, (iii) the design of a new ventilated hat, and (iv) an improvement in the selection of workers. While many studies have been carried on the optimization of load-carrying ability of a person, the studies in relation to the standardization of lifting load are scanty in our country. Recently computer simulation human model has been used for the evaluation of manual material handling operation (Nag & Pradhan 1991) and centre of gravity analysis in load-carrying operation (Hingorani & Ray 1991). A detailed study on the different manual material handling operations in the Indian Army has been started for optimization of load-carrying and load-lifting operations of the soldiers (Majumdar 1993).

Physical Fitness and Maximum Physical Work Capacity

Maximal work capacity (MWC) as indicated by maximum O_2 uptake were determined in groups of industrial workers on a bicycle ergometer. The MWC in warm and very hot conditions was found to be as much as 45% lower than that at comfortable conditions (Sen *et al.* 1967, 1969). The occupational work capacity as related with MWC revealed very poor status of physical fitness in young Bengalee students as compared to that of westerners mainly due to bad food habit, absence of physical exercise etc. (Sen *et al.* 1973, 1974).

Evaluation of battle field physical efficiency of the troops at high altitudes is extremely difficult. Six hundred troops in the age range of 17-45 yrs were studied at the plains and altitude up to 4000 m using hill climbing distance of 3 miles with ascent and descent of 300 m as formulated by Malhotra *et al.* (1966). The evaluation of physiological fitness status and performance capacity of mountaineering students (Ramaswamy & Purkayastha 1970) and fire-fighting personnel in Defence Services were also carried out. It was recommended that step test score and the dyspnic index can be used as screening test for assessing the performance potentialities of the mountaineering students.

The induction of sojourners to moderate to high altitude show deterioration in physical work capacity and the level of deterioration varies with respect to the physical fitness status of the individual prior to induction. The effect of physical training on work capacity and adaptation to altitude was studied by a number of workers incorporating the relationship of physical standards with endurance (Nayar *et al.* 1982) and to formulate specific training programme based on physiological responses for the maintenance of operational efficiency of our soldiers (Mathew *et al.* 1983)

Anthropometry and Body Composition

Metabolic rate, energy cost and oxygen consumption are expressed per unit of body surface area or body weight or lean body mass in either sex. Based on the actual measurements, new constants were suggested for both the weight-height formula and the different body segments in the linear formula (Banerjee *et al.* 1958), and a nomogram

was constructed for convenience of calculation from the body weight and height (Banerjee & Sen 1957).

Estimation of body composition by direct method at high altitude including body density measurements were made on 100 soldiers along with other anthropometric measurements like skin fold thickness and circumference at various sites of the body, along with body weights. Stepwise linear regression equations were derived relating 36 anthropometric measurements of body density and lean body weight. The weaker correlation coefficients in the regression equations were explained as individual variations of subcutaneous fat which is common at high altitude (Bhardwaj *et al.* 1976). An anthropometric survey of Indian Army personnel including 62 body measurements were carried out to arrive at proper sizes of clothing and personal equipment for protective measures (Bhardwaj *et al.* 1984).

A similar study was carried out on 2072 Indian Naval personnel. Twenty-six anthropometric and 21 clothing measurements were selected for this purpose. Twenty-five sizes for tunics, trousers and shirts and 13 sizes for half-sleeve shirts have been provisionally selected for introduction in the Indian Navy (Bhardwaj & Zachariah 1992). Later an attempt was made to reduce the number of half-sleeve shirt sizes of the Indian Army from the existing 13 to 9 for better inventory management. A re-analysis of the body measurements of 4800 soldiers was made; divided into 9 size groups based on chest and waist girths. The response regarding the fitment trials were found encouraging (Zachariah *et al.* 1993).

Anthropometric measurements were also taken in male workers of the western India to help in the designing of textile equipment and machinery (Sengupta & Sen 1964). Sen (1964) measured 41 different anthropometric dimensions on normal naturally acclimatized subjects consisting of males, females and children from eastern part of India. On comparison, it was observed that there was a significant difference between the body form of the people in tropical country and those in cold climates, presumably to provide greater evaporating surface. The difference in the BMR of these subjects and those of the cooler climates was much less than expressed in terms of unit cell mass or cell solids. This indicated that heat production mechanism is also on a lower gear and has significant bearing on combatting the heat load by the Indian workers. Sen & Ray (1978) have also determined the whole body mineral content of Indians, which were found to be influenced by the nutritional status.

Environmental Factors

Thermal Environment. It is well known that the body temperature of a man must be kept within narrow limits in order to maintain both the physical and mental health. In various types of industrial, agricultural and military work the thermal environment imposes a considerable amount of heat load on the workers or soldiers to reduce efficiency and productivity.

Sen (1965) stated that different physical factors which affect the health of the industrial workers are to be considered carefully. The factors include the physiological principles governing thermal effects, the evaluation of heat stress, prescription of upper tolerance limits, disorders due to heat, their treatment and prevention, the effects of noise, vibration etc.

A detailed investigation on incidence of heat illness was carried out on 4000 troops in the desert. The Indian soldiers, including the Gorkha troops, were found to be well acclimatised to heat and could stand strenuous military training under 34°C Wet Bulb Globe Temperature (WBGT) or dry bulb temperature of 40°C. Sweat rate up to 1.9 kg h^{-1} was recorded. The water requirement of troops while engaged in different physical activities under varied environmental conditions was evaluated on heat acclimatised subjects in summer months. An equation, $W = 0.416\ (X\text{-}15)$, was developed for the calculation of daily water requirement, where W is the regular fluid requirement in litres and X is the WBGT in degree centrigrade (Anon 1969).

Various thermal indices such as WBGT index, modified effective temperature (ET) index and predicted four-hour sweat rate (P4SR) were evaluated to assess the relative efficiency of these indices in relation to physiological responses while working in hot environments. The three heat stress indices were equally well correlated with the physiological responses (Venkataswamy & Lal 1970). Prehydration was found to be most beneficial in reducing physiological strain. At least 50% restoration of sweat loss has to be allowed for prolonged work in hot environment (Pichan *et al.* 1986).

Other complex acclimatization phenomena such as human responses in cross adaptation in heat, cold and noise (Joseph *et al.* 1983), role of potassium supplementation and renin-angiotensin-aldosterone system during exercise in heat were studied in depth and specific recommendations have been made (Sridharan *et al.* 1987).

It would seem that as the body composition, environmental condition etc. of Indians are quite different from those of the Westerners, a new set of different thermal indices are essential for the Indian workers, apart from the existing thermal standards laid down by the Westerners.

Noise. The damaging effect of noise on human performance has created an increased awareness on the researchers, industrialists and defence personnel. The number of studies carried out in our country on the effect of noise on human systems in the civilian sector are far more less than in the Westerners. In comparison, a number of studies were carried out on the Indian Army, Navy and Air Force personnel, to evaluate the effect of intense noise on performance and communication in the field situation and the effectivity of different ear plugs and ear muffs. Ammunition noise generated from main or small bore gun is more intense and damaging than industrial situation. Malhotra *et al.* (1968) found varying magnitude of hearing loss in Navy personnel.

The sound level, frequency analysis, and auditory effect of high intensity noise on tanks crew (Rai *et al.* 1977), Artillery and Armoured corps personnel (Rai *et al.* 1978) were evaluated to design the safe period of exposure and recommending proper ear defenders. The efficacy of indigenously made sonex and perforated stainless steel disc ear plugs were tested along with other commercially available ear defenders. Sonex ear plugs showed highest attenuation quality at 4 and 6 kHz as compared to others. Studies were also carried out to find out the role of bandwidth and centre frequency on the development of temporary hearing loss (Chaturvedi *et al.* 1983). Singh *et al.* (1982) compared blood pressure and heart rate of 75 soldiers exposed to occupational noise of 88-107dB(A) for 10-12 yrs with 36 nonexposed normal subjects. Irregularity in cardiac rhythm, both in amplitude and duration, was found in 18% of the exposed subjects as against 6% in the nonexposed group. Exposed group showed lesser degree of vasoconstriction in the hand blood flow and slower recovery rate. Biochemical evaluation of the effect of noise on the group of subjects revealed significantly higher levels of free cholesterol, Y-globulin and cortisol in the exposed group (Rai *et al.* 1981).

The effect of carbogen (95% O_2 plus 5% CO_2) in the protection against noise-induced hearing loss, as prophylactic in the development and recovery of TTS and as therapeutic agent in the recovery of sensorineural hearing loss were studied in detail (Chaturvedi *et al.* 1990). Carbogen appeared to be highly effective and useful in these conditions.

Sports and Work Physiology

Higher levels of physiological performance in the modern world athletics and sports persons is achieved by improved training techniques with the help of physiological integration in various body functions. Such physiological assessments for selection and training of athletes and sportsmen are quite common in developed countries but are very limited in our country. Studies have been conducted on Indian athletes, sportsmen, boys and girls of different age groups with a view to ascertaining the factors responsible for poor performance in this field.

Simultaneous changes in oxygen consumption, blood lactic acid and ionic concentration, ventilation, haemoglobin, RBC, WBC, specific gravity of blood, heart rate, blood pressure and electrocardiographic components were observed in rest, submaximal and maximal work on both male athletes and sedentary students of Calcutta University of age group of 17-22 yrs by Maitra *et al.* (1968). Proportionate changes were noted with graded work for ventilation, oxygen consumption and lactic acid production only. Maitra *et al.* (1968) further studied the physiological responses to muscular activity at two different temperatures of 28°C and 30°C and concluded that in warm humid condition, oxygen consumption, heart rate and blood lactate concentration were increased than those at lower temperature.

Several other pioneering studies have been carried out during the last two decades

to observe the changes in the relative and actual concentrations of serum protein fractions in response to treadmill running (Banerjee *et al.* 1969), the variations in vital capacity, maximal breathing capacity and Harvard step up test score in athletes and nonathletes (Banerjee *et al.* 1970), effect of vitamins B and C on the physical fitness of athletes (Chatterjee *et al.* 1977), and effect of physical training during adolescence period on maximal aerobic capacity (Chatterjee *et al.* 1979). A number of studies have evaluated the maximum aerobic capacity in sprinters of young girls and boys (Banerjee *et al.* 1982) and of college women (Chatterjee & Chakraborty 1986). It was observed that the sprinters, pentathelets, javelin throwers and jumpers did not differ significantly from each other but each group was significantly superior to basket ballers, hand ballers, badminton players and swimmers (Chatterjee *et al.* 1991).

Chatterjee & Mandal (1993) studied the physical and motor fitness level of Indian school-going boys and showed that these fitnesses increased with advancement of age. Major increment were recorded between 14 and 15 yrs of age. An alternative to regular physical exercise, the effect of yogic exercise in the improvement of muscular efficiency (Ray *et al.* 1986) and body flexibility (Ray *et al.* 1986) in middle-aged men were studied in detail on healthy soldiers aged 40-48 yrs. It was observed that the practice of selected 'Hatha' yoga exercise can increase the muscular endurance and delay the onset of fatigue.

Ghosh *et al.* (1991) evaluated the physiological demand of amateur boxers of three different categories and concluded that although the aerobic capacity of the boxers may differ in different weight category yet the physiological demand of the game remained the same. Goswamy *et al.* (1991) used a simple string diagram for the measurement of the movement pattern of five badminton players. An attempt has also been made to develop regression equations for the simple and quick method of estimation of oxygen debt (Sengupta *et al.* 1974), maximum aerobic power (Verma *et al.* 1977), human endurance time (Verma 1993).

Future Perspective

In the Indian context, the ergonomic consideration of new equipment/tools developed and to be used in different environmental conditions may be a thrust area. Short-term improvement programme includes design of low-cost personal and public transportation systems for rural and urban areas and simultaneous improvement of existing systems such as rickshaws, hand carts, buses, railway coaches, driver's cabin, housing, schools and school furnitures, hospitals, agricultural and industrial tools, consumer products and mass education programmes. The long-term areas are large anthropometric survey, development of heat stress indices suitable for use in tropical countries, establishing threshold limit values for toxic substances under the particular work conditions in India, proper work organizations improving health promotion, safety and environment of the industries.

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NUTRITION

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Nutritional sciences are an important area in which several original and epoch-making contributions have been made by Indian scientists, during the last 75 years. This brief report attempts to summarise some of the important contributions in the field of nutritional physiology that have been made in several leading laboratories in the country. While highlighting contributions made both in basic animal experimental studies and in clinical, applied or human investigations, an attempt has been made to explain their relevance and to outline the emerging trends in several major thrust areas in this field.

ANIMAL EXPERIMENTAL STUDIES

Major contributions have been made by Indian scientists in the field of *nutrition and brain development.* Several laboratories in the country and in particular scientific groups at the National Institute of Nutrition (NIN), Hyderabad, MS University, Baroda, Christian Medical College, Vellore and the Indian Institute of Science, Bangalore have made outstanding contributions to our understanding of the neurochemical changes that occur in the developing brain as a result of early malnutrition. It is not the purpose of this review to outline in detail the contributions made in neurobiochemistry of undernutrition or malnutrition in animals since there are several recent reviews doing precisely this (Sastry 1989).

More recently, *electrophysiological studies* have been conducted at the All India Institute of Medical Sciences (AIIMS) by Usha Nayar's group during postnatal growth of undernourished rats that showed that undernutrition caused a retardation in the neuronal activity of the cerebellum (Puthuraya *et al.* 1980a). They also described changes in visual evoked potentials, reduction in conduction velocity of sciatic nerves and in numbers and sizes of motor neurons of gastrocnemius muscle (Puthuraya *et al.* 1980b). Working on the ontogeny of feeding Mathur *et al.* (1983, 1986) showed that neurons of rat ventromedial hypothalamus developed normal glucose activity at about 21 days of age which could be advanced to 15 days of age by administering glucose to the rat pup from fifth day of age. LH neurons showed opposite effects. Desiraju and his group at the National Institute of Mental Health and Neurosciences (NIMHANS), Bangalore studied the changes occurring in the course of ontogeny of visual and motor cortices of the rat using electrophysiological, morphological and neurotransmitter assessment during undernutrition. An initial lag in the development of the undernourished brain was followed as the rats grew older by an excess development

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in some of the parameters which were considered as being of an adaptive nature in these undernourished animals. They also showed that nutritional rehabilitation had little effect in preventing the consequences of early undernutrition. These studies on *neurophysiological changes in early undernutrition* in experimental animals by both these groups have been summarised by Desiraju (1989).

Sharma's group in University College of Medical Sciences, Delhi have extended the electrophysiological studies to human subjects. Non-invasive evoked potential recording techniques have been used to establish sensory involvement of brain in malnourished states. Different grades of protein-calorie malnutrition in infants and children affected absolute and interpeak latencies of brainstem auditory evoked potentials (BAEPs). Impairment was more in infants, particularly in rostral pathways as compared to children with same degree of malnutrition (Tandon *et al.* 1989). In children having B12 deficiency anaemia waveform of BAEPs was found to be indistinct and with low amplitude and on vitamin therapy BAEPs showed considerable improvement (Tandon & Choudhary 1990). Visual evoked potential (VEP) study has revealed subclinical involvement of visual pathways in some vit.A deficient cases even before clinical signs of xerophthalmia manifest themselves in the eye (Tandon & Ram 1993). The extent of xerophthalmia has been correlated with type of VEP abnormality and its reversibility on parenteral administration of vit.A. These evoked potential studies have served as a potential tool in diagnosing subclinical cases even before clinical manifestations of nutritional deficit start appearing, and may have considerable significance in management.

Ramakrishna's group at Calicut University have been studying the effects of single deficiencies of the B group vitamins (thiamine, riboflavin and pyridoxine) on the *development and maturation of electroretinograms* (ERGs) in rats. They demonstrated very elegantly a significant reduction in thickness of the retina, in particular the ganglion cell layer, in pyridoxine-deficient pups which caused a delayed ontogeny of the normal (ERG) characteristics, resulting in a delay in the development of depth perception and exploratory behaviour in these B6 deficient rats (Mukkadan & Ramakrishna 1982).

No treatise on the neurophysiological studies in undernourished animals is complete without reference to the elegant studies on *sensory physiology and undernutrition* carried out by Sharma's group at St. John's Medical College, Bangalore in the period mid-1960s to mid-1970s. Sharma's group demonstrated changes in gustatory, gastric and intestinal chemo- and mechano-receptor activity following varying grades of undernutrition in animals (Sharma 1972). These studies contributed to our understanding of sensory physiology and hlghlighted the important role played by the vagus and sympathetic components of the autonomic nervous systems in modulating the activity of these receptors in undernutrition (Sharma *et al.* 1972). It was brought out that while chemosensory signals from food provide the sensory basis of hedonic matrix that controls food acceptance, choice and intake (Sharma *et al.* 1977), these sensory and nutrient signals from food are also intimately involved as primary biological variables.

These studies thus extend the behavioural work on sensory/metabolic model of food intake (Jacobs & Sharma 1969), and broaden the electrophysiological work on the role of nutritional state in autonomic modulation of alimentary afferent system (Sharma 1972, Sharma *et al.* 1972, Sharma 1975).

Savithrama *et al.* (1978) studied the histomorphology and cholinesterase activity of the taste buds and the gustatory nerve fibres in well-fed, in protein and protein-calorie deficient rats. The nerve fibre arborisation in the taste buds is predominently non-myelinated and shows degenerative changes ranging from initial swelling to disintegration, fragmentation and finally complete disappearance with the increasing degree and duration of food deprivation. Coincident with these changes in the nerve fibre, the taste bud also shows various stages of degeneration. By contrast, the cholinesterase activity in the gustatory papillae shows an initial increase during the first week followed by a decline in the activity during the succeeding weeks; a second peak of cholinesterase activity appears during 4-6 weeks. The cholinesterase activity is barely detectable after the 8th week. In the more severely protein-calorie restricted groups, the cholinesterase changes are more pronounced and abrupt in onset and show a total disappearance by 4-5 weeks.

Biochemical, histochemical and gustatory profile studied to investigate the response of gastrointestinal mechanisms to a graded deprivation in the calorie intake and meal-time restriction of rats showed differing results (Sudha & Dua-Sharma 1989). Gustatory tests showed an increase in the intake of glucose and saccharine in all the groups (moderate, severe calorie restricted and meal-time restricted). Females appeared to have a better discriminative capacity than the males showing over-reaction to gustatory stimuli. They appear to be predisposed for sensory regulation facilitated by effects of gonadal hormones after sexual maturity. Females during the ovulatory phase together with reduced calorie intake have a higher discriminating power than males and females in the non-ovulatory phase. Gradation in the activity of mucosal enzymes from oral to aboral end was seen. While activity was enhanced in meal-time restricted/moderate calorie restricted rats, severely restricted showed a distinct decreased response, showing the existence of a critical level of adaptation. Intra-luminal factors, namely food, are important for the enzyme response as shown by the results of the Thiry-Vella loop segment as compared to the segment in continuity in well-fed rats. The studies point to the possibility that under conditions of undernutrition and severe calorie restriction adaptive changes of intestine take place and are also reflected in feeding behaviour responses like oral sensory cues. Changes manifest during early development may influence the adult pattern of food response.

Although most of the work has been on animal models, and the bridge between electrophysiological events and food-related behavioural events is far from being completely understood, the analysis of the general problem of the role of sensory and nutrient signals, input control and energy exchange in the overall continuum of undernutrition – surfeit states, is potentially as applicable to man as to the rat (Sharma *et al.* 1979).

In recent years studies on effects of chronic food deprivation interacting with afferent neural signals have revealed a multistage organisation in which the 'energy pool' or the state of nutrition biases the signalisation pattern in a manner that the individual gathers and analyses the information and reacts in strict accordance with the requirements of external and internal environment (Radhakrishnan & Sharma 1988, Kravstov *et al.* 1991). The flow of information to the brain is not all in one direction. The sensory and metabolic properties of food or the energetics of the system are germane in initiating and sustaining the activities of the organism so that the basic urge or the need of the individual is differentially interfaced with motivational systems for activating drives to satisfy the need and thereby regulate the purposive behaviour (Sharma 1992).

During the past two decades Selvamurthy and his colleagues at the Defence Institute of Physiology and Allied Sciences (DIPAS), Delhi have carried out studies on the *nutritional requirements of soldiers* in different environmental and operational conditions. All the ration scales for the three wings of our Armed Forces, soldiers on patrol duty, fresh recruits (Malhotra *et al.* 1976), submariners, various tradesmen and pioneers working in Border Roads Organisation (Ilavazhagan *et al.* 1989, Sridharan *et al.* 1987), Coast Guard personnel and boys studying in Military Schools and Sainik Schools (Sridharan *et al.* 1984) have been formulated by this Institute. The recommended scales are already in use at the national level. The nutritional requirements of patients of different categories have also been provided to the military hospitals based on studies carried out by the above researchers.

The requirements of soldiers differ from the normal civil population because they may have to work in the extreme environments like high altitude (Srivastava 1992), cold, deserts, under water and in aerospace. They have routinely a high level of physical activity. Considering these, recently a study has been carried out to evaluate the vitamin requirements at extreme high altitude of troops depending on processed tinned food, which is the normal practice due to short supply of fresh food items in these areas. Earlier studies by DIPAS had shown high calorie requirements at altitudes above 4000 m. This needs to be met by enhancing the fat component of the food. Rai *et al.* (1975) assessed the utilisation of different quantities of fat at three altitudes 3500 m, 3800 m and 4700 m respectively. It was observed that the digestibility of fats was not affected up to intake of 364 g of fat per day. The gastrointestinal functions are not severly affected up to an altitude of 3500 m (Sridharan et al 1982). It was also seen that the supplementation of either vitamin C or vitamin A helped in the process of high altitude adaptation. The problem (Ilavazhagan 1989, Grover *et al.* 1985) of hypophagia at high altitude is extensively studied both in animal models and in human volunteers to explore the possible mechanisms of both physiological and psychological nature, due to reduced food intake at high altitude (Sridharan *et al.* 1984). Use of healthy food as adaptogens facilitates the process of acclimatisation and ameliorates the effects of stress (Srivastava 1992).

Experimental studies in animal models of early undernutrition have over the last

two decades focused on *energy metabolism and thermoregulation* and have been carried out at St. John's Medical College, Bangalore and the National Institute of Nutrition, Hyderabad. Studies carried out at St. John's demonstrated changes in basal metabolic rates (BMR). and non-shivering thermogenesis (NST) in preweaning undernourished pups from large undernourished litters which resulted in their inability to thermoregulate when exposed to cold (Muralidhara & Shetty 1988). Nutritional rehabilitation reverses many of these changes although the animals tended to remain stunted and failed to achieve full catch-up growth despite nutritional rehabilitation. Related work carried at the NIN, Hyderaboad showed that gain in weight and body fat was lower in previously energy-restricted rats. Studies on varying protein content of the diet also showed that low protein diets (12%) resulted in higher BMRs and NST responses as compared to high protein (20%) and diet-restricted animals (Mohan & Rao 1983).

In view of the role played by brown adipose tissue in NST, the influence of *nutritional status on the development of adipose tissue* (both brown and white) and adipocyte morphology in albino rats was also investigated at St. John's Medical College, Bangalore (Jasthi, 1991). Pinto & Shetty (1993) have investigated the role of increased maternal physical activity during pregnancy and lactation on the pregnancy outcome and nutrition in the pre-weaning period. In addition to showing that increased maternal physical activity has deleterious effects on birth weight and growth of pups, they also showed that these effects are carried over to the next generation even if the mothers had not exercised during pregnancy. The effects of undernutrition seem to have inter-generational consequences and influence several generations of offspring.

Experimental studies in animals and man conducted in AIIMS in recent years have indicated that supply of metabolizable fuels is critical for full expression of thermogenic capacity and administeration of amynophylline (AMPY) improves the cold tolerance in fasted state by enhancing substrate mobilization and also increasing thyroid activity. A study conducted to compare the thermogenic action of AMPY in preweaning and postweaning undernourished rats indicated that AMPY treatment significantly improved thermogenesis in preweaning than in postweaning rats. The effect of acute cold exposure an substrate mobilization showed that undernutrition limits glycogenolysis in muscle and liver but not in brown adipose tissue at any age and promotes lipolysis. AMPY improved thermogenesis by shifting the metabolism towards lipolysis. The increase in thyroid hormone levels associated with increased blood glucose and free fatty acid levels indicated participation of T3 and T4 in thermogenic effect of AMPY (Sachdeva *et al.* 1990).

The experimental animal studies summarised here are far from complete since no attempt has been made to include the range of animal studies being carried out in nutrition which may have a more biochemical basis such as those related to nutrition and brain development, nutrition and cataract, nutrition and urolithiasis, or animal models of osteoporosis, much of which have been investigated by several laboratories in the country and in particular at the NIN, Hyderabad.

CLINICAL AND HUMAN STUDIES

For obvious reasons, the contributions of Indian scientists to our understanding of the physiological mechanisms and the pathophysiology of undernutrition and malnutrition based on clinical and human investigations have been outstanding. These contributions go back for several decades and once again the NIN at Hyderabad leads in this area with its Diamond Jubilee coinciding with that of the Academy. Many of the important contributions made after the 1920s have been summarised earlier by Gopalan (1970a,b).

Our understanding of the *pathophysiology of protein-energy malnutrition* in children and why malnutrition in children manifests clinically either as Kwashiorkor or marasmus and that their evolution is related not to the composition of the diet but to deficincies in the pathophysiology of the endocrine adaptive process is a significant contribution made at the NIN (Gopalan 1968). The failure of an adequate adreno-cortical response during protein-energy malnutrition in children leads to Kwashiorkor; a suppressed or poor response being seen even during the stress of infection while elevated ADH levels contributed to the oedema seen in these children. Kwashiorkor in childhood was also associated with elevated levels of growth hormone and low somatomedin activity unlike marasmus. Although BMRs of both children with Kwashiorkor and marasmus were lowered, only children with Kwashiorkor had lowered thyroid function status. The important studies made in the *endocrine functions of childhood malnutrition* indicated that protein-calorie malnutrition was associated with functional alterations in endocrine gland function with endocrine glands working at a lower level of activity and demonstrating an inability to respond to acute stress or stimulation along with the responses of tissues to hormonal action being altered. Studies carried out at NIN also reported a poorer *mental performance* of *malnourished children* which did not show adequate 'catch-up' in longitudinal follow up. Studies on mental function, physical work capacity and nutritional status of school children have also been carried out by Agarwal's group in Varanasi (Agarwal *et al.* 1987).

Other physiological studies in nutrition carried out at the NIN, Hyderabad relate to the minimal protein intake for maintaining nitrogen balance, estimations of endogenous faecal nitrogen losses and iron and other nutrient losses by sweating in the tropics particularly following profuse sweating during heavy physical exercise. BMR changes during pregnancy and lactation, energy expenditure of agricultural and other occupation groups, and body composition changes in adult malnutrition are some of the other important physiological contributions made at the NIN during the same period (Gopalan 1970a,b). Pioneering work on measurements of basal metabolic rate of Indians were also carried out by Krishnan & Vareed in Madras (1932), by Sokhey & Malandkar in Bombay (1939) and other groups which were elegantly summarised by Banerjee (1962). Banerjee has also made several measurements related to the energy expenditure of rickshaw pullers, loaders and manual labourers as well as body composition measurements in normal adults.

Other significant contributions in this field were related to *establishing growth standards* of well-to-do children showing that well-nourished children in India have growth rates and attain heights and weights nearly similar to those of American and British children (ICMR 1978). More recently studies coordinated by Agarwal (Agarwal *et al.* 1991) support the same observation that the growth potential of well-nourished Indian school children is not different from that of children in the West.

An area that has been investigated extensively in the last decade was on the whole a question of whether *metabolic or physiological adaptation in energy metabolism* contributes to lowering energy requirements of undernourished adults who have relatively low habitual energy intakes. Results of such investigations have enormous implications to our understanding of energy requirements and estimation of numbers of undernourished people who are considered to be below the poverty line worldwide. Investigations on undernourished adults using whole body indirect calorimetry to implicate physiological mechanisms involved in this adaptive process have been summarised recenty (Shetty 1993). These studies showed that although a reduction in BMR was seen in undernourished and underweight adults (Soares & Shetty 1991), the finding of a lowered oxygen consumption per unit of active tissue mass, considered a hallmark of increased metabolic efficiency and hence a sign of metabolic adaptation, was difficult to prove. If in fact such changes occurred they may actually reflect changes in body composition, in particular the proportion of muscle to non-muscle tissue that contribute to the active tissue mass. Studies from Shetty's laboratory also showed that both non-shivering and dietary induced thermogenesis did not reflect any adaptive advantage to the undernourished individual (Shetty *et al.* 1993). Changes in energy cost of physical activity implied if anything an ergonomic advantage, perhaps the result of habituation rather than any specific physiological advantage during exercise. Studies carried out at the NIN showed that the *energy cost of exercise* was not altered and if anything mechanical efficiency was lowered in undernourished adults (Satyanarayana *et al.* 1991). *Work output* both in agricultural and industrial situations seemed to be lower in undernourished individuals with compromised anthropometric features such as lowered body weight, stature and body mass index (Satyanarayana *et al.* 1979). The existence of metabolic or physiological adaptation in undersourished adult was thus elusive and difficult to prove and thus contributed little to variations in energy requirements of such individuals.

Autonomic nervous system tests and cardiovascular responses have been investigated in undernourished adults and have indicated a lowered sympathetic drive, associated with enhanced receptor sensitivity and an enhanced parasympathetic activity (Vaz *et al.* 1992). These have been followed up with the state-of-the-art studies using norepinephrine kinetic studies in humans (Vaz *et al.* 1994). These may result in alterations in the pharmacokinetics and the pharmacodynamics of several agonist and antagonist drugs which may be of enormous clinical significance. Outstanding contributions on *altered pharmacokinetics of drugs in malnourished adults* have been made earlier by Krishnaswamy (1983) who studied the pharmacokinetics and pharmacodynamics of a whole range of drugs such as antipyrine, phenylbutazone,

chloroquine, acetyl salicylic acid, sulphadiazine, tetracycline and streptomycin in malnutrition.

Studies on the *physiological role of dietary fibre* have been carried out at St. John's in the 1980s. Kurpad & Shetty (1986) have summarised their studies on human volunteers that showed that starch supplementation in the diet altered intestinal transit time, increased faecal bulk and faecal nitrogen excretion; so did administration of antibiotics which affected the colonic bacterial flora, while activated charcoal had no effect on any of the parameters studied. Studies at AIIMS by Bijlani's group looked at the effect of source and type of dietary fibre on *glycaemic response* in human subjects (Siddhu *et al.* 1989) while at NIN fenugreek was investigated for its ability to lower the glycaemic response to glucose (Sharma 1986).

This review on physiological studies related to nutrition in humans is far from exhaustive. It highlights the important developments and contributions made over the last several decades. Our understanding of protein-calorie malnutrition and the patho-physiological mechanisms related to its evolution have emerged from the work of Indian physiologists. So has the appreciation that metabolic adaptation contributes little to alter the energy requirements of undernourished adults and has thus exposed the fallacy of the argument that adults on low intakes are possibly meeting their energy requirements by enhancing their physiological efficiency. Indian physiologists have contributed to the worldwide database on basal metabolic rates of adults and children as well as pregnant and lactating women, a parameter which is now accepted as possibly the best available method to estimate energy requirements of individuals and population groups both in the country and globally (FAO/WHO/UNU 1985). Such contributions which were made by several groups of investigators from the 1920s to the 1990s also include measurements of energy cost of physical activity, which has also been added on to the global database and is being used by international agencies such as the WHO and FAO (James & Schofield 1990). Physiological measurements of growth of children and adolescents have helped establish national reference standards for growth of Indian children. There is little doubt that physiological studies in nutrition have been a major contributor to the entire gamut of scientific endeavour of the physiological community in India.

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CIRCADIAN RHYTHMS

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Circadian rhythms are ubiquitous and are basic to existence of life on this planet. With the exception of bacteria all organisms investigated express circadian rhythms in their physiology (Bunning 1973). Even so chronobiology, study of circadian and other biological rhythms, became respectable as scientific pursuit only in 1960 (Chovnick 1960) and the first monograph on the subject was written only in 1958 (Bunning 1958). Considering the delayed recognition of circadian rhythms, as the very sign of vitality and adaptability of life on earth, research in this area has made commendable progress in India. In the present chapter, only landmark and important papers published by Indian scientists in the period 1979-1993 have been considered. The cut-off date for the earliest papers is arbitrary and the idea is to consider only major scientific advances.

The Madurai group lead by Chandrashekaran began research work on the circadian rhythms in 1975. The experiments on microchiropteran bats *Taphozous melanopogon* on which R. Subbaraj wrote his Ph.D. thesis (Subbaraj 1980) was very well received. Work by this group may best be summarized as dealing with "bahavioural expressions of biological clocks" and the early papers dealt with the effect of light on the circadian rhythms in the flight activity of these bats. Subbaraj & Chandrashekaran (1981) demonstrated for the first time on a vertebrate system mirror-imaging phase response curves for the circadian rhythm of a bat with steps of light and darkness. This was followed by a series of papers in which Marimuthu and Chandrashekaran reported that there was a case for "social entrainment of the circadian rhythm in the flight activity of the cave-dwelling bat *Hipposideros speoris* (Marimuthu *et al.* 1981) and that this social entrainment may even turn out to be species-specific (Marimuthu & chandrashekaran 1983) and that the spectacular social synchronization wherein the darkness of a true cave "bat tells bat time" is abolished by LL (Marimuthu & Chandrashekaran 1983). Dilip Joshi, working also on the bat *Hippo speoris*, reported in a series of papers daylight dimmer than starlight (0.0001 to 0.0006 lx) entrains the circadian rhythm and the first daylight phase response curve obtained for the circadian rhythm of a bat inside a natural cave (Dilip Joshi & Chandrashekaran 1983), the shortest light flashes of 0.5 ms resetting the clock (Dilip Joshi & Chandrashekaran 1984). Dilip Joshi also reported on the spectral sensitivity of the photo-receptors responsible for phase shifting the circadian rhythm in these bats (Dilip Joshi & Chandrashekaran, 1985). N. Viswanathan reported in another series of experiments that there is a maternal behavioural entrainment of the circadian rhythm in activity and rest of pups in the field mouse *Mus booduga* (Viswanathan & Chandrashekaran 1985), how LL abolishes this impressive maternal entrainment and the limits to this maternal

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entrainment (Viswanathan & Chandrashekaran 1988).

Subbaraj and colleagues investigated the responses of the starling circadian system to transitions from light to darkness and also reported on the effect of imipramine and amitriptyline on the circadian locomotor rhythm in the field mouse *Mus booduga*. Since 1987, the Madurai Group has been working on "human circadian rhythms" in a specially constructed isolation facility. Work of this nature has been done in W. Germany, the U.K., the U.S.A. and Japan. Chandrashekaran *et al.* (1991) discovered and reported for the first time that "the menstrual cycle in the human female is not coupled to the circadian rhythm of sleep-wakefulness in social isolation". In another paper they reported a "direct correlation between the circadian sleep-wakefulness rhythm and time estimation in humans under social isolation" (Chandrashekaran *et al.* 1991). These experiments on human circadian rhythms are being continued.

Another leading laboratory has been that of Professor J.P. Thapliyal in Varanasi, where among a dozen Indian endocrinologists and chronobiologists, Asha Chandola – Saklani, eminently stands out and was trained in the field of avian endocrinology, circannual rhythms and circadian rhythms. Pavgi & Chandola (1981) demonstrated an interesting photoperiodic control of seasonal reproduction in a tropical weaver bird and the role of gonadal feedback (Singh & Chandola, 1982). They further demonstrated the effect of LD cycles and food intake in the daily rhythmicity in body weight of spotted munia (Bhatt & Chandola, 1981). In a series of papers they showed seasonal variations in photogonadal responses and reported on reproduction strategies in birds in tropics which involved the interaction of photoperiod and circadian/circannual rhythms (Chandola *et al.* 1985). It was further reported (Pant & Chandola-Saklani 1992) that "pinealectomy and LL abolished circadian rhythms but did not alter circannual reproductive or fattening rhythms in finches". The latest discovery from their laboratory is "a role for thyroid hormones in the development premigratory disposition in the red-headed bunting" (Pant & Chandola-Saklani 1993). Migratory disposition itself arises out of complex interactions between circadian rhythms and environmental photoperiod and possibly, in addition, circannual rhythms. In recent years Asha Chandola-Saklani has also increasingly turned her research interests to the areas of game management, captive breeding and conservation measures of Himalayan wildlife and pheasants and has published extensively on these topics.

Another group of active workers has been that of A.K. Pati and collaborators in Raipur University, who earlier worked in Banaras Hindu University and were trained in the laboratory of Prof. J.P. Thapliyal.

Thapliyal *et al.* (1981) reported the involvement of the thyroid in the circadian rhythm of oxygen consumption of the spotted munia. Whereas Pati & Thapliyal (1983) showed a chronosusceptibility of ophidian blood variables to pentobarbital, and a circannual variation in the timing of eonsinophil circadian rhythm in snakes (Pati & Thapliyal 1984), Pradhan *et al.* (1985) also detected a phototactic rhythm in a cave fish and a circadian rhythm in surface activity (1985b). A.K. Pati has also worked on

cortisol circadian rhythms documented in samples of saliva and venous blood from healthy human subjects (Touitou *et al.* 1986). He further reported alterations of circadian rhythms in lymphocyte subpopulations of patients with hematological malignancies (Canon *et al.* 1986). Pati & Saini (1991) recently reported desynchronization of oral temperature, pulse and performance circadian rhythms, in shift-working Indian nurses and more recntly the group reported that "the internal clock undergoes acceleration in healthy nurses on night shifts". It must be pointed out however that their conclusion was based on data obtained on 10 s interval time estimations made once every 4 h. It is doubtful if subjective time estimations of such short duration of 10 s are truly coupled to the circadian rhythm at all (Chandrashekaran *et al.* 1991).

Researches of Professor P.D. Tewary's group at Banaras Hindu University and Vinod Kumar at Meerut University (initially both from Prof. J.P. Thapliyal's laboratory) have also contributed to several aspects in this field. Tewary & Kumar (1981a, 1981b, 1981c) demonstrated the involvement of a circadian periodicity in the induction of gonadal growth in the black-headed bunting *Emberiza melanocephala* and in the photoperiodic responses in the male common Indian rosefinch *Carpodacus erythrinus* (Tewary & Kumar 1982). Vinod Kumar has continued to publish several papers with P.D. Tewary as co-author on experimental manipulation of photoperiod and induction or termination of seasonal phenomena implicating in all cases circadian mediation in the black-headed bunting and the Indian rosefinch (Kumar & Tewary 1982a,b, 1983, 1985, Kumar 1986a,b, 1988). Working in Professor B.K. Follett's laboratory in Bristol, Vinod Kumar reported on the circadian nature of the photoperiodic clock in the Japanese quail (Follett *et al.* 1992) and on the circadian rhythm in melatonin secretion in this bird (Kumar & Follett 1993). Vinod Kumar has written an account in 1993 on the phase response curve for 1 h light pulses for the circadian rhythm in plasma concentrations of melatonin in rams.

Dr. V. Reghunandanan and colleagues of Rohtak Medical College have published a few interesting papers on the effect of lithium and a vasopressin antagonist and ethanol injected into the suprachiasmatic nuclei of rats (Reghunandanan *et al.* 1987, 1988, 1989) and have also reviewed the possible role of vasopressin in circadian time keeping (Reghunandanan *et al.* 1990).

Light serving as a synchroniser of circadian and other rhythms linked to diurnal and seasonal light dark variations serving as a reliable clock to schedule reproductive functions, migrations, metabolic activities etc. is well known. The trend of the modern photo-physiologic concept has been the realisation that the action of light via retina, hypothalamus and neuro-endocrine system plays an important role in guiding behaviour (Sharma *et al.* 1992). There is emerging histomorphological and electrophysiological evidence establishing retinal projections to hypothalamus, midbrain and limbic structures and explain the role of visual cues in light-induced complex functions in higher forms. Working on the possible neural mechanisms involved in photo-endocrinal control and circadian rhythms, Sharma's group at University College of Medical Sciences, Delhi (Nagar *et al.* 1988) strongly suggested the possible relationship between Infundibular

Nucleus (IN) of hypothalamus, optic system and the pituitary. Exposure to continuous light induces prolonged estrus in rat. The effects appear to be mediated through retino-hypothalamic-pituitary axis resulting in the stimulation of pituitary gonadotrophs and MSH secretion. Prolonged light exposure increases the activity of neurons in IN while destruction of the hypothalamic region abolishes the estrus response.

This brief summary of the work on circadian rhythms being carried out cannot for obvious reasons be exhaustive. Any omission may please be understood as unintended oversight.

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RESEARCH ON YOGA

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In recent years there has been considerable interest in scientific research on yoga in India and in the West. However, it is heartening as well as interesting that the earliest research on this ancient Indian science began in Lonavala (Maharashtra). The meticulous work which also involved X-ray studies was carried out by Swamy Kuvalayananda (Kuvalayananda 1925a,b), who demonstrated intravisceral pressure changes as well as shifts in the relative positions of the viscera during *kriyas* or cleansing procedures. After this, for a while yoga research was focussed on investigating physiological potentials and some unusual claims of yogis being able to lower their metabolism (Anand *et al.* 1961a), to shut off sensory stimuli while meditating (Anand *et al.* 1961b), and their ability to alter their cardiovascular functions at will (Anand *et al.* 1961c, Wenger *et al.* 1961, Kothari *et al.* 1973).

In the early 1970s a new dimension was given to research on yoga when the epoch-making study by Wallace (1970) showed that the practice of Transcendental Meditation brings about a "unique hypometabolic physiologic wakeful state" with overall signs of psychophysiological relaxation. The seventees also witnessed a spate of research work conducted in various laboratories of India primarily directed to study the variety of physiological changes occurring in common man during yogic practices. Detailed experiments on the physiologic effects of diverse practices (e.g. asanas) have been conducted in Lonavala (Bhole 1970). A study from DIPAS (Delhi) showed that six months training in *asanas* (physical postures), *pranayama* (breathing practices), and meditation brought about definite physiological changes in normal volunteers, viz. an increase in orthostatic tolerance and an overall shift in the autonomic equilibrium towards parasympathodominance, as was shown during Transcendental Meditation (Selvamurthy *et al.* 1983). However, more recently, work done at the Department of Neurophysiology, NIMHANS (Bangalore) has revealed that descriptions of overall effects of yoga practice such as a reduction of sympathetic activity are not to be expected. Different variables such as the pulse, skin resistance and heart rate can be expected to change differently when the same subject practises yoga (Telles & Desiraju 1993). These findings are in accordance with known views of autonomic response and individual specificity (Engel 1960).

Most of the other research on the physiological changes during yogic practices have been confined to specific parameters. The cardiac recovery index (CRI) assessed

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by the Harvard step test was shown to increase after 2-1/2 months of yoga training (Muralidhara & Ranganathan 1982). Six months of yogic *asanas* were also shown to increase hip and shoulder flexibility in the middle-aged men whereas physical exercises had no such effect (Ray *et al.* 1983). Nayar *et al.* (1975) demonstrated improvement in cardiorespiratory functions in NDA cadets trained in yogic practice as compared to those undergoing physical training. The body flexibility and the muscular efficiency improved after six months of yogic training (Ray *et al.* 1986). The improvement in muscular efficiency was reflected as an increase in endurance time probably due to alternate recruitment of motor units. Besides, yogic practice could result in a significant improvement in physiological responses to acute cold exposure by facilitating the process of non-shivering thermogenesis (Selvamurthy *et al.* 1988). Yogic practices have also been found useful in improving biological markers of ageing. Aroor and co-workers (Aroor *et al.* 1990) reported significant increase in cardiac efficiency index, vital capacity, creatinine clearance and decrease in blood glucose and urinary excretion of catecholamines after one month of yogic practices. Reports of energy expenditure and ventilatory responses to *siddhasana* have shown greater minute ventilation, larger tidal volume, higher O_2 consumption, greater CO_2 elimination, and higher heart rate in sitting posture as compared to horizontal-supine and chair-sitting postures (Rai *et al.* 1994). The results suggest that *siddhasana* is a mild type of exercise and may have its applications in conditions of low cardiorespiratory reserves particularly in individuals in whom heavy exercises are contra-indicated.

There has also been considerable research work on biochemical changes during yogic practices. The studies conducted at the Banaras Hindu University (Varanasi), showed that 6 months of yoga practice increased 17-hydroxycorticosteroid excretion, reduced serum cholesterol, blood sugar and increased serum proteins (Udupa 1972, 1985). These findings (specially the increased adrenocortical activity) were interpreted as increased stress competency. Later, at DIPAS Santha *et al.* (1981) described the biochemical changes indicating a relative hypometabolic state along with reduction in sympathetic activity. Investigating the role of sahajyoga in stress, Rai and his colleagues (Rai *et al.* 1989) studied blood lactic acid, urinary vinyl manddic acid blood pressure, heart rate and respiratory rate in subjects trained in sahajyoga, and observed a significant decrease in these parameters. Galvanic skin resistance, on the hand, significantly increased indicating a state of relaxation.

The long-term practice of Transcendental Meditation was shown to alter pituitary hormones (e.g. TSH, LH) and cortisol responsiveness to LH-RH and insulin, respectively (Ahuja *et al.* 1981). A report (Sahay *et al.* 1982) from the Vemana Yoga Research Institute (Secunderbad) showed an increase in creatine phosphokinase and reduced pyruvate to lactate ratio following 3 months of yoga practice.

When these studies on the physiology of yoga were being carried out, research efforts were also directed to assess the therapeutic potentials of yogic practice in stress-related, psychosomatic ailments, particularly hypertension, hyperthyroidism, ischaemic heart disease, acid peptic disease and ulcerative colitis (Udupa 1976). Though Datey

other diseases. Nine months of practising the integrated approach of yoga therapy (described above) significantly improved the IQ and social adaptation of 45 children with varying degrees of mental retardation, compared to a matched control group who did not practise yoga (Uma *et al.* 1989). These children also showed a marked improvement in their concentration and eye-hand coordination as assessed by a steadiness test, within 10 days of yoga practice (Telles *et al.* 1993).

Training in yoga is also useful to cause significant reduction in visual and auditory reaction time, increase in breath holding time and hand grip strength (Mohan *et al.* 1992). Fortunately, certain organisations (such as the Mitra Mandal, Maharashtra) have attempted to disseminate this training for the benefit of society, by teaching yoga to jail inmates with encouraging results (Vyavahare 1991).

In conclusion, it must be mentioned that studies on physiological changes in yoga can actually be the basis for an in-depth understanding of changes in neural processes with altered states of consciousness. For example, studies on sensory cerebral evoked potentials have already revealed that specific brain areas (i.e. thalamic nuclei) are principally involved during the relaxed state and alertness maintained while practising pranayama (Telles *et al.* 1993). It can thus be seen that diverse aspects of yoga and its applications have been studied in India, and that there is an interesting and potential scope for future research.

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ENVIRONMENTAL PHYSIOLOGY

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The Indian subcontinent presents a wide spectrum of environmental profile including climatic conditions, terrain and meteorological factors. The environmental features range from alpine climate over the Himalayas, tropical desert along the western part over Rajasthan, hot humid climate over the soutern peninsula and humid forests with high rainfall over the eastern part. These regions are inhabited by people of different ethnic origin with varying anthropometric, socio-cultural and traditional habits including food, clothing etc. In view of the wide diversity of the climatic conditions as well as ethnic variations, the research in the field of environmental physiology assumes great importance in the Indian context. In addition there are civilian native inhabitants also living up to an altitude of about 4,500 m. Recently in some of these high altitude areas tourists are also permitted to visit some locations. In view of the above, some of the primary research institutions in the country like Defence Institute of Physiology and Allied Sciences (DIPAS), Defence Institute of Psychological Research (DIPR), All India Institute of Medical Sciences (AIIMS), University College of Medical Sciences (UCMS), Delhi, and Desert Medicine Research Centre (ICMR), Jodhpur, have been working on these problems.

ENVIRONMENTAL PHYSIOLOGY

Adaptation to different environments is primarily determined by both genetic factors and physiological mechanisms regulating various body functions. The environmental physiology research in India have focussed attention on the adaptation of biological systems including men, animals and plants. In the description to follow the focus has been laid on the adaptation of men to different environments, as well as some of the research related to the influence of climate on animal productivity since India has the largest animal wealth.

High Altitude Environment

Northern frontiers of India are located mostly over the Himalayan ranges where a large number of armed forces personnel need to be deployed even up to altitudes slightly above 5000 m. In addition, there are considerable numbers of native population inhabiting altitudes up to about 4500 m. Every year many mountaineering expeditions attempt to scale cliffs of Himalayas as an adventure sport. Recently the influx of tourists and trekkers has increased to these isolated snow-clad mountainous regions. In view of the above, the focus on High altitude (HA) physiology has assumed significance, particularly after the sixtees.

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Research groups in the Defence Research and Development Organisation and Director General, Armed Forces Medical Services spearheaded these research efforts. Earlier efforts by the Defence Institute of Physiology and Allied Sciences (DIPAS) were to formulate an acclimatization schedule to reduce the mortality and morbidity of troops and find prophylactic measures to prevent maladaptation problems (Nair & Gopinathan 1971, Nair *et al.* 1971, Chohan *et al.* 1977) like Acute Mountain Sickness (AMS), High Altitude Pulmonary Oedema (HAPO) and cold injuries. The DIPAS scientists have studied many physiological problems related to safe tenure of posting at HA, nutritional requirements, load carriage and physical efficiency on acute induction and during acclimatisation (Srivastava 1992, Srivastava & Ratan Kumar 1992).

Pathophysiology of HAPO was first reported by Menon (1965) and efforts were made by Singh & Chohan (1973) to explore the potentials of diuretics as prophylactics against maladaptation. Paintal (1969) reported the significant role of J-receptors in the pathophysiology of HAPO and has given a new concept for its pathophysiology. Vishwanathan *et al.* (1969) in V.P. Chest Institute found an attenuated cold pressor response in patients of HAPO, while Mathew *et al.* (1983) at DIPAS reported a lower chemoreceptor sensitivity in patients of HAPO and AMS. Roy *et al.* (1969) at the AIIMS found altered cardiovascular responses in maladapted individuals. Chohan *et al.* (1977) reported certain aberrations in clotting mechanism which may perhaps play a contributory role in the pathophysiology of maladaptation. Even some chromosomal changes were observed on prolonged stay at high altitude (Bhardwaj *et al.* 1987).

In the last decade, the emphasis shifted towards understanding the neurophysiological mechanism underlying the acclimatisation at HA (Selvamurthy 1984). Their recent studies show that shift in autonomic balance towards sympathetic overactivity and subsequent build-up of parasympathetic tone are important components of altitude acclimatisation (Selvamurthy *et al.* 1981). EEG changes show cerebral cortical synchronisation due to hypocapnia induced by hyperventilation during initial phase of induction (Selvamurthy *et al.* 1978). Similarly, the short frequent arousals and reduction in slow wave sleep are beneficial to prevent accentuation to hypoxemia due to sleep hypoventilation (Selvamurthy *et al.* 1986). A new concept was proposed to illustrate the possible involvement of neurogenic mechanism in the genesis of HAPO (Selvamurthy 1989), and the potential application of yoga (Selvamurthy *et al.* 1988) and ayurveda (Srivastava & Ratan Kumar 1992) in preventing altitude maladies. The native population in most of these studies serve as standard model of adaptation for comparison (Selvamurthy 1988).

The hormonal profiles were studied in sojourners during acclimatisation at HA and compared with those of the acclimatised lowlanders and natives (Sawhney *et al.* 1991). Thyroid hormones showed a relatively higher activity of thyroid in sojourners (Sawhney & Malhotra 1991). However, the thyroid handling of radio-iodine at HA presented an oscillatory pattern, while the natives presented a stable pattern (Rawal *et al.* 1993). Besides the physiological responses, the sojourners also show varying degrees of psychological responses like anxiety, depression, emotional instability, decline in

concentration, short-term memory and mental efficiency (Sharma *et al.* 1976). Exposure to moderate altitude, on the other hand, is reported to have some beneficial biomedical applications also (Selvamurthy 1993).

Cold Stress

Northern part of India including Himalayan ranges experience cold in winter months. It reaches sub-zero temperatures in the Himalayan ranges. DIPAS has carried out research on acclimatisation to cold. A three weeks of cold acclimatisation schedule formulated by DIPAS is in vogue at the Himalayan ranges for the sojourners. The physiological characteristics of cold acclimatisation were illustrated on tropical men by following the above schedule, by using standard cold test at 10°C with only shorts on, and recording cardiovascular and metabolic parameters including shivering (Mathew *et al.* 1981). These responses could be modulated by the practice of yogic exercises, which was seen to improve thermoregulatory responses by facilitating non-shivering thermogenesis (Selvamurthy *et al.* 1988).

Cold Injuries

Frostbite is a common form of cold injury among the sojourners at HA. Efforts are directed towards its prevention and therapy as well as to identify the susceptible individuals. Vitamin C combined with rewarming at temperatures ranging from 37° to 41°C in water medium or tea decoction is found to minimise the extent of injury after the cold exposure. The cold-induced vasodilatation (CIVD) appears to be a useful test for predicting susceptibility (Purkayastha *et al.* 1992).

POLAR PHYSIOLOGY

Indian physiologists have participated in polar expedition to both the arctic and antarctic environments. The physiological responses like biorhythm, sleep, thermoregulation, hormonal profile, physical and mental efficiency were studied on sojourners (Purkayastha *et al.* 1993). Arctic experiments included the native population also for comparison. These experiments showed that it is possible for tropical Indians who hail from low latitudes accustomed to hot environment and about 12 h of light-darkness cycle, to get acclimatised to the arctic environment with extreme cold and altered solar periodicity. Intial acclimatisation takes about 5 weeks. The circadian rhythm of physiological functions shows a slight shift of acrophase to the left and reduction in the amplitude of oscillation (Ray *et al.* 1993). Sleep disturbance was noticed during the days of geomagnetic disturbance. The hormonal profile and other related physiological and psychological responses were studied by the physiologists of AIIMS, New Delhi. The cold exposure to the body core is a prerequisite for acclimatisation. If an individual resorts to avoidance of cold exposure by remaining in temperature-conditioned environment, there is little chance of physiological acclimatisation. The handling of snow or cold water and cold exposure are also reported to improve the peripheral vascular response to cold thereby protecting the

acclimatised individuals from cold injuries (Purkayastha *et al.* 1992).

Usha Sachdeva and her colleagues at AIIMS have reported (1994, personal communication) on the extremes of cold temperature, frequent geomagnetic storms, blizzards, the unique day-night cycle, high levels of radiations that are some of the natural hostile conditions to which the antarctic expedition members are faced. The psychosocial factors such as marked sensory deprivation, social isolation, small close-community, hypodynamia during winters further complicate normal human activity and behaviour at polar station.

One of the most important factors affecting human activity in antarctic is the quality and vitamin content of food. Sporadic research on nutritional aspect of members in antarctic have yielded conflicting reports. The control studies done during X and XI Indian antarctic expeditions have indicated increased body weight of all the members despite the monotony of frozen tasteless food which was artificialy supplemented with vitamins and minerals. This evidently enables one to predict that there is reorganization of human body metabolism under these conditions and even with inadequate vitamins and minerals the polar scientists maintain a steady body weight. A study is being conducted on XIII antarctic expedition members to determine the glycemic index of precooked frozen foods consumed by the polar scientists and correlate this with their body composition. The information gained would help minimize the metabolic problems and thereby improve the performance of expedition members.

Heat Stress

India being a tropical country experiences heat stress in different parts. It is present either as dry heat over the western part (Rajasthan) or humid heat over the southern peninsula. Many laboratories are engaged in research in understanding the physiological responses to heat and its correlation to health and efficiency. DIPAS has carried out extensive research in this area. The hypohydration above 2% is observed to result in decline in physical and mental efficiency (Selvamurthy *et al.* 1993). The water adjustment in different body fluid compartments during different levels of dehydration and rehydration show interesting patterns (Singh *et al.* 1993). Sodium availability in tropical diet is adequate to meet its loss in sweat and hence there is no additional requirement for its supplementation (Pichan *et al.* 1988). On the other hand, potassium supplementation is required to maintain optimal efficiency. Preventive measures for avoiding heat casualties have also been proposed (Pichan 1989).

In recent years, Desert Medicine Research Centre at Jodhpur has been established by ICMR and the institution has embarked on a series of studies aimed to address mainly physiological problems encountered in desert region. More particularly, these cover (i) health survey and surveillance, (ii) physiology of adaptation, (iii) environmental health problems, and (iv) collecting and updating information on impact of desert conditions on living systems. Attempts are on to set up desert health monitoring system and desert health informatics. Field studies are being extensively conducted to assess,

among others, pulmonary functions in respiratory problems in desert. While cases of occupational silicosis which are found in sandstone quarries of desert have been reported, efforts to investigate whether cases of non-occupational silicosis occur in desert of Rajasthan are also on. It seems people suffer from non-occupational silicosis (desert lung syndrome) because of the presence of a large number of stone quarries spread all over. Urolithiasis is another condition markedly found in population of Jodhpur and adjoining areas and raises possibility of its linkage to environmental conditions of arid zone (ICMR 1993).

In the desert region of western Rajasthan the air temperature during peak summer goes up to 45-47°C with low relative humidity, high wind velocity and insufficient recharging of groundwater. All these factors result in poor productivity of the land. It might seem paradoxical that the desert region which puts so many hurdles for life should harbour such a vast number of livestock as the Great Indian Desert does. Obviously animals indigenous to this tract have been fairly successful in adapting to their habitat. One of the major mechanisms is conservation of water through decreased insensible means, urinary and faecal water loss, and role of rumen as a water reservoir. Investigations by Khan & Ghosh (1989) on animal adaptation to desert environment have brought out a number of interesting features. It was reported that the effects of standard grazing stress on body weight maintenance, daily water intake, total body water (TBW) and body water turnover (BWTR) in goats and sheep indigenous to Rajasthan desert during summer, showed increased BWTR both in goats (7%) and sheep (12%). The BWTR of goats is less as compared to that of sheep and suggests goat's superior adaptability to withstand thermal stress under desert conditions. It is known that animals in arid zone are not able to dissipate heat during day-time by radiation, conduction or convection. They may rather depend on the expensive water evaporative cooling.

AEROSPACE AND UNDER-WATER PHYSIOLOGY

The Institute of Aerospace Medicine, Bangalore and Institue of Naval Medicine (INM), Bombay are engaged in research related to medical and physiological problems related to aerospace and under-water environments. The selection of cosmonauts is done using specific physiological and psychological coordinates using simulated environments (Dikshit *et al.* 1984). The psychophysiological problems of diving and submariners are being studied by INM and DIPR.

MICRO ENVIRONMENTS

In the micro environments like dwelling units, occupational environments like factories, and crew compartment of armoured vehicles in military situations, the personnel are likely to be exposed to noise, vibration, toxic fumes, air ionisation etc. Even electropollution due to microwaves, electromagnetic waves, radio-frequency waves, lasers etc. have received the attention of physiologists. Our Indian physiologists at DIPAS, Jawaharlal Nehru University (JNU), UCMS, Delhi, Indian Toxicological

Research Centre (ITRC), Lucknow, and Institute of Magnetobiology, Madras, are working in these areas. Exposure to electromagnetic field in extremely low frequency has many beneficial effects for treatment of patients, besides its effects on physiological responses manifested in ECG, EEG and respiration (Subrahmanyam *et al.* 1987). Microwaves exposure in chamber lead to modulation of immunity (Nageswari *et al.* 1991), while the radio frequency waves also modulate some neuro-physiological response and behaviour (Mathur *et al.* 1988). Environmental pollution is another problem where ITRC, Lucknow and UCMS, Delhi are working, besides DIPAS (Satija *et al.* 1978, Chaturvedi *et al.* 1984, Jeevaratnam & Selvamurthy 1990, Gupta *et al.* 1993). For details reader is referred to the Section on *Industrial Pollution and Work Place Environment*, published in this monograph.

All these studies give a glimpse of a wide spectrum of research in the field of Environmental Physiology in India, and clearly indicate the potential importance of enlarging the scope of activity and follow the studies in a systematic manner.

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INDUSTRIAL POLLUTION AND WORK PLACE ENVIRONMENT

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Environmental pollution has become a global concern and attempts are being consistently made to minimise its hazardous effects. The earth summit held at Rio-De Janerio in June 1992 in Brazil is a good example of such efforts. While depletion of protective ozone layer from the atmosphere has been linked to environmental pollution, the major contribution to the present-day plight is the industrial emission both to external and internal environment along with vehicular density. No doubt the growth of industries, particularly in developing countries, is an index of their prosperity, such industrial growth appears to be heading towards a state by which human life is perilously close without their fault of having been exposed to such polluted environment while working and more drastically when one becomes victim of industrial accidents or nuclear power plants. The plight of people belonging to metropolitan cities is somewhat different where thousands of substances are daily dispersed into the air, and where each breath of air is really a dilute cocktail of chemical and particulate matter of uncertain and variable composition (Gerrit WHS 1980). The work place environment, e.g. dusts, vapours and fumes, has a more direct effect and further adds to the environmental hazards. This has been realised over the centuries. As early as in second century A.D., the miners had realised the impact of work place environment and they covered themselves with sacks and used animal bladder as masks to protect themselves from dust. But it was not until 16th century that medical interest in disease associated with industry began with observations by Agricola. Bernardino Rammazzini (18th century), rightly acclaimed as Father of Occupational Medicine, pointed out the importance of asking about a patient's work when considering his illness and emphasized that "to the question recommended by Hippocrates one more should be added, `What is your occupation?' (Davis *et al.* 1977).

The list of potentially hazardous substances is very long and respiratory system being directly communicating with external environment suffers from a wide variety of lesions ranging from simple bronchitis to cancer of lungs. Interestingly, the size of the particulate is quite important to know apart from its chemical nature, as we human beings can inhale up to 10 μm size particles, and the smaller the particle the deeper it penetrates, having a high residual time and causing its injurious effects to the lung tissues accordingly.

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THE INDIAN SCENE

In India a rapid and unplanned mushrooming growth of industries has come into existence over the last few decades specially in and around metropolitan cities as these polluting industries have moved from developed to developing nations (Samet & Spengler 1992). The prominent ones are cotton, jute, metal, rubber, tobacco, stone-cutting, along with mining industries. Obviously, location of these units depends upon availability of raw material. Prevalence of cotton and diamond industries is much more on the west coast of India (Bombay and Gujarat), jute industries are in the east coast (Bengal), coal mines are in Bihar, whereas metal, rubber and stone-cutting are in both south and north India. The distribution of tobacco and pan masala units is not restricted to a particular zone of the country.

The recognition of occupational health hazards as an emerging field by Indian scientists may be traced to early sixties with the pioneering work in textile workers of Gujarat by K.C. Gupta and his co-workers who showed the presence of byssinossis in them (Gupta & Kulkarni 1963). Since then a number of studies have been undertaken and full-fledged centres established at various places so that systematic research work in an organised manner could be carried out in the right direction. These establishments are mainly associated with known national bodies like National Institute of Occupational Health (ICMR) at Ahmedabad, Industrial Toxicology Research Centre at Lucknow (CSIR), Institute of Environmental Research and Management (IERM), Gorakhpur, Department of Chest Medicine & Environmental Pollution Research Centre, Bombay, and such institutions are also situated at other places in India. In addition, work is being conducted in several institutions, particularly on epidemiological, sociological and pathophysiological aspects of environmental pollution. One such centre which has recently come up is the Division of Environmental Physiology, University College of Medical Sciences, Delhi.

Industrial Toxicants

Work on byssinosis, first identified by K.C. Gupta and his team (Gupta & Kulkarni 1963), was later studied in detail to define the extent of deterioration in lung functions (Kamat *et al.* 1981) and histamine release along with correlation with anthropometric measurements and physiological responses on small airways (Rustogi 1993).

Pneumoconiosis is a well-known devastating disease prevalent in miners and it is often in combination with tuberculosis. In India it is well documented by the pioneering work of Biswas *et al.* (1973) who showed that there is decrease in ventilatory lung functions of workers as compared to nonworkers. Stone mines are located at various places in India through which we get granite (north & south), marble (north) and of other kinds of stones. These workers who are involved in cutting, picking, breaking and loading are liable to suffer from silicosis. Gupta *et al.* (1969) carried out lung function assessments and chest X-rays in them depicting restrictive pattern of lung functions along with silicotic changes in lungs.

Although exposure to asbestos is not so common in India because still the quantum of central air-conditioning and other usages in institutions or factories or offices are not so common, yet the pattern of lung functions along with abnormal findings of chest X-rays clearly throws light on the dose-effect relationship in asbestos workers who suffer from various grades of asbestosis (Shah *et al.* 1983).

Diamond-cutting and polishing is quite a common business in northern parts of India but hardly any work on these workers is available in the Indian literature except of A.L. Anand (1984) who carried out roentgenographic survey in 750 workers, depicting a high prevalence rate of tuberculosis in them. He further concluded that causative factors for such states could be dusty working environment, poor nutrition and over-work.

The workers of talc industries, located in Rajasthan near Udaipur, were extensively studied (Damodar 1984). These workers are found to be exposed to soapstone dust (while grinding) comprised of 55-62% silica as silicate, 28-32% magnesium oxide, 0.75-1.5% calcium oxide, 0.1-3% ferric oxide and 3-6% aluminium. Apart from ventilatory lung functions (FVC, FEV1 & FEV1%) their chest X-rays were also studied. These studies indicated the presence of air flow limitations of varying degrees in the workers, depending on the duration of soapstone dust exposure.

Chest diseases are quite common amongst tobacco handlers as well as in smokers for which importance of smoking index for assessing lung damage by lung function tests (LFT) has been worked out by A.K. De *et al.* (1989). Their study indicated reduced lung function values while matched with non-smokers, and the degree of reduction of LFT was found to be increased with smoking index (SI). To get exposed to a high concentration of coal dust (consisting of calcium, silicate, magnesium, aluminium, iron and free silica) is a common phenomenon while working with boilers and turbines in thermal power plants. These workers have been studied for their ventilatory lung functions (Rajgopal & Doshi 1988, Chattopadhya *et al.* 1992) and were found to have tremendous decrement in pulmonary lung function tests related to the duration of exposure.

Recently workers of an iron foundry were assessed in terms of work place environment by using five-stage preseparator for Total Suspended Particulate (TSP) and its fractions and the presence of heavy metals in TSP as well as in their fractional components. All the lung function tests except TL (Transfer factor of lung) were measured, and P.A. view of X-ray chest of these workers was carried out. The decrease in flow rates in group of workers (mixing unit) along with varied abnormal X-ray chest findings were found to be proportionate to the high concentration of work place pollution to which these foundry workers were exposed (Gupta *et al.* 1993a).

There are countless products prepared out of rubber and while processing the raw rubber, a number of chemicals, resins, powders, soaps and dyes are added. Some of the industries in East Delhi manufacturing tyres and tubes on a large scale (supplying their

products not only all over India but export also), have been studied. It has been observed that there is heavy pollution in the mixing units as compared with vulcanising and packing-loading sections. The presence of PAH (polynuclear aromatic hydrocarbon) compounds make the whole environment not only injurious to health but may contribute towards high mortality rate. These workers showed abnormal increase in airway resistance, residual volume (RV), RV/TLC ratio, decreased flow rates and other lung volumes and capacities as compared to normal subjects belonging to similar anthropometric and socio-economic status. Their X-ray chest also exhibited presence of abnormalities ranging from prominent broncho-vascular markings to pleural effusion along with Koch's lesions. These results including presence of varied signs and symptoms were proportionate to the quantum of pollution and duration of work to which these workers were exposed (Gupta *et al.* 1993b,c). These workers were also compared for their lung functions with the workers, handling talc, tobacco, coal ash, oil residue, rice, saw mill, slate pencil, wool carpet and metal, who showed various restrictive and obstructive lung functions which appear to be pollution-dependent.

Industrial accidents

Accidental exposure of human race to disastrous materials including radioactive substances as in the case of Chernobyl in 1986, explosion of tanks holding radioactive waste in Siberia in 1993, gushing out of thousands of litres of irradiated water from reactor at Tarapur in 1978 and damaged unit I of atomic power station in 1981 at Kota, Rajasthan and to industrial toxicants in Bhopal in 1984, are not uncommon as many other such occurrences may pass out without being noticed. However, it is worth mentioning about the world's worst industrial accident that occurred in India on 3 December, 1984, when 30 tons of methyl isocyanate and other chemicals were released into the air. As expected, this led to the development of various respiratory problems (Misra *et al.* 1987) including pulmonary edema (Sharma & Gaur 1987). Follow-up of affected persons confirmed lung function derangements to the magnitude of prevalence of restrictive (78%) and obstructive pulmonary defects (29%) along with inability to maintain normal minute ventilation and oxygen uptake at rest (55%) in the exposed patients (Kamat *et al.* 1985, 1987). Apart from pulmonary injuries ophthalamic ailments were not uncommon and ranged from photophobia to corneal ulceration (Dwivedi *et al.* 1985). Bhandari *et al.* (1990) showed abnormal reproductive responses in females having high rate of abortion (24.2%) as compared to non-exposed (5.6%) population, indicating some sort of mutagenic developments in them.

Indoor Toxicants

Another important cause of pollution is biomass, fuelwood, crop residues and animal dung, used daily in about half the households of the country for cooking and heating purposes. In the process large amounts of air pollutants are released, when these are burnt in simple household stoves which have low thermal efficiency and high emission factors. The biomass smoke contains respirable particulates, CO, formaldehyde and hundreds of other simple and complex organic compounds, including PAH. In a

growing number of air pollution monitoring studies, it has been shown that the resulting human exposures to those pollutants often exceed recommended WHO levels by factors of ten, twenty or more (Pandey *et al.* 1989). It has also been found that in developing countries the poor population is much more exposed to such hazardous pollutants (Pandey *et al.* 1988). In recent years, there have been some studies that directly focus on these households. The quantity of air pollutants generated during the burning of bio-fuels depends on combustion parameters like type of fuel, stove and ventilation. A series of experiments have been carried out in laboratories and simulated field conditions (Dave 1984) to measure the emission factors and concentration of these pollutants. The results of the studies carried out on stoves using wood as fuel on three improved metal stoves clearly indicate that the highest thermal efficiency is fuel-dependent. Further, the emission factors for both TSP and CO in improved metal stove are higher in most cases when compared with those unvented metal stoves. However, on a per task basis, the emission of one or both pollutants was lower in some improved stove fuel combinations. Hence, a trade-off exists between improvement in efficiency and increase in emission. In a recent study, the emmission of TSP and CO from biomass combustion (Khandpal *et al.* 1991) also showed that it is linear with the increase in the feeding rate (fuel consumption). Though these studies give a good estimate of the concentration of these pollutants, field measurements are necessary to study the actual impact of indoor pollutants on human health.

Biomass smoke is known to cause serious health effects such as lung diseases, eye irritation, acute respiratory infection (ARI) etc. ARI, as pneumonia, is one of the chief killers of children belonging to developing countries, and reporting of such cases could be 4-5 million per year and this figure is quite close to figures for other diseases like diarrhoea (Monto 1990). A relationship between exposure to atmospheric biomass smokes and suffering from ARI was worked out in Indian children by Rao *et al.* (1992). Recently impact of domestic cooking fuel was studied (Behera & Jindal 1991) by recording various respiratory symptoms in 3,701 women. Out of these, 3608 were non-smokers and used biomass, LPG kerosene and mixed fuel to cook their food. Presence of high % of respiratory symptoms was observed in those females using mixed fuel (16.77%) followed by chulla (12.5%), stove (11.4%) and LPG (9.4%). The overall respiratory symptoms were 13% in all groups of women. Further, chronic bronchitis in chulla users was significantly higher than with kerosene and LPG users (<0.05%). Chronic obstructive lung diseases are also extensively studied in India and other neighbouring countries (Behera & Jindal 1991, Pandey 1984). Their results clearly indicate that smoking is a major contributory factor amongst the population studied. Gupta *et al.* (1988) also reported not only deterioration in ventilatory lung functions in females but frequent complaints of behavioural changes and development of headache in those housewives using kerosene stoves as compared with others using LPG stoves. Recently Saxena *et al.* (1992) conducted a detailed study on the impact of TSP and CO on human population, comprising adults, youths and children of either sex. It was observed that indoor micro-environment was a major contributory factor to the daily integrated exposure than the outdoor microenvironment.

Future Perspective

One may suggest that there is a dire need to improve the industrial environment in terms of checking emission from these units and prevent the suffering of people. To initiate the process a constant health monitoring cell in each hospital is recommended for these industrial workers. Simultaneously, improved stoves must be designed so that their thermal efficiency increases with inversely related emission of pollutants. One will have to aim at improving both the household and external environment and also the work place environment of industrial units.

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